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THE TWENTIETH ANNIVERSARY OF THE DISCOVERY OF ARTIFICIAL RADIOACTIVITY

A. P. Ratner

Twenty years have passed since one of the most important discoveries of the twentieth century – the discovery of artificial radioactivity by Frederic and Irene Joliot-Curie. While studying the transmutation of elements during their bombardment with alpha particles from polonium, the Joliot-Curies noticed that three elements – aluminum, boron and magnesium – emitted positrons under the action of polonium alpha particles. The radiation did not come to an end even after the cessation of the bombardment, and its intensity decreased exponentially with time in the same manner as that of natural radioactive elements. The Curies explained this phenomenon by the fact that, as a result of transformations caused by alpha particles in the nuclei of these elements, unstable radioactive nuclei decomposing with the emission of positrons were formed. They verified the correctness of their hypothesis by using the fact that the artificially obtained radioactive nuclei were different in their chemical properties from the elements which were bombarded.

Actually, the nuclear reactions which took place in the Curies' experiments can be written in the following form, taking into consideration the fact that neutrons are emitted in these reactions:

$$Al_{13}^{27} + He_2^4 \rightarrow P_{15}^{30} + n_0^1,$$

$$B_5^{10} + He_2^4 \rightarrow N_7^{13} + n_0^1,$$

$$Mg_{12}^{24} + He_2^4 \rightarrow Si_{14}^{27} + n_0^1.$$

The Joliot-Curies isolated the radioactive isotopes of phosphorus P^{30}, nitrogen N^{13}, and silicon Si^{27}, which were obtained as a result of these reactions, from the bombardment target, after having previously added small amounts of inactive isotopes of these elements, and showed that all the activity was concentrated in the added carriers. Thus, they were the first to artificially prepare and isolate new radioactive isotopes of ordinary elements which do not exist in the radioactive form in nature.

It would be hard to overestimate the value of the discovery of Frederic and Irene Joliot-Curie for all of modern science. It is sufficient to say that they provided the original impetus for investigations that led to the discovery of nuclear fission (to which, incidentally, the Curies also made a very important contribution) and to the possession of nuclear energy by humanity.

The discovery of artificial radioactivity had especially great significance for chemistry. It has made possible the extending of the field of application of radioactive methods in chemistry, previously limited by the framework of the natural radioactive elements, to the whole of the Periodic System.

The extraordinary sensitivity and specificity of radioactive methods (they can easily determine radioactive isotopes in quantities of 10^{-12}–10^{-18} g in a great mass of extraneous matter, including inactive isotopes of the same element) have been used for a long time for the solving of a number of experimental problems in various fields of chemistry. It is sufficient to recall the synthesis of the hydrides of the heavy elements of the IV and V groups, carried out by Paneth, the determination of the coefficients of diffusion of lead in metal and in a number of salts, the investigation of the metabolism of lead and bismuth in the organism, etc. However, the greatest possibilities which radioactive methods open up for experimenters could not be utilized to a sufficient extent as long as their use was limited to the ten elements at the end of the periodic system for which natural radioactive isotopes are known.

After the discovery of artificial radioactivity the preparation of artificial radioactive isotopes of the stable elements became possible; at the present time, we have such isotopes for almost all elements in quantities sufficiently great for their wide utilization. Thanks to this, unlimited possibilities for the utilization of radioactive methods in various fields of chemistry have been opened up; in recent years they have found their widest use, their applications increasing with every year.

Even the most concise statement of all of the results achieved in chemistry through the use of artificial radioactive elements would be far too long, not only for this article, but even for a large monograph; we will therefore limit ourselves to the citation of some of the most important examples which will make it possible for us clearly to realize the importance of the use of artificial radioelements in chemistry.

First, it is necessary to cite the discovery of new chemical elements. Even the utilization of natural radioactive elements had made possible the discovery of a series of new elements, the radioactive isotopes of which were encountered in nature in insignificantly small quantities. These elements occupied the places which had been empty in the periodic system between bismuth and uranium, with the exception of the two elements with the atomic numbers 85 and 87 – ekacesium (astatine) and ekaiodine (francium).

The discovery of artificial radioactivity made possible a significant increase in the number of known elements and the extension of the borders of the periodic system, since it enabled us to obtain radioactive isotopes of previously unknown elements and to study their chemical properties by radioactive means. Certain new elements, e. g. plutonium and technetium, which were discovered and the chemical properties of which were first investigated by radioactive methods on insignificantly small quantities of them, were then isolated in weighable quantities and their chemical properties studied by ordinary chemical means; the conclusions made on the basis of radiochemical investigations were, as a rule, fully confirmed.

The first new transuranium elements, discovered through the use of the phenomena of artificial radioactivity, were neptunium, Np, Z = 93, and plutonium, Pu, Z = 94. They were discovered by American radiochemists in 1940-1944 among the artificial radioelements which were obtained by the bombardment of uranium with neutrons. Even the first work on the chemical properties of the newly discovered elements, carried out on the short lived isotopes Np^{239} and Pu^{238} on quantities on the order of $10^{-13}-10^{-14}$ g made possible the establishment of the great similarity between the chemical properties of the new elements and uranium. This led to the conclusion that the last elements of the periodic system begin a new group of elements which are analogous in their properties to the rare earth elements. The formation of this group is associated with the completing of the inner 5_f electron shell. Later investigation with weighable quantities of these elements fully confirmed this conclusion, and if there is still a difference of opinion among chemists on this question it is only on whether this group begins with actinium or uranium.

Soon, by means of the bombardment of uranium and plutonium with quickly moving deuterons and other heavy nuclei, Seaborg was able still further to extend the borders of the periodic system, discovering elements one after another; they were: Americium, Z = 95; curium, Z = 96; berkelium Z = 97; californium, Z = 98; and finally, in 1951, afinium, Z = 99, and centurium, Z = 100. The discovery of the latter two elements was recently confirmed by American and Canadian scientists.

Artificial radioactivity made possible not only the extending of the borders of the periodic system to Z = 100, but also the filling of the empty places in it. After the discovery of rhenium and hafnium, there remained four empty places in the periodic system – the rare earth element Z = 61, ekamanganese, Z = 43, and the two elements mentioned above with Z = 85 and 87. By the selection of the corresponding nuclear reaction, radioactive isotopes of these elements were obtained; this made possible the study of their chemical properties. The isotopes of element number 43, which is called technetium since it was the first artificially obtained element (1937), have long lives ($Tc^{99}T = 2.1 \cdot 10^5$ years,, $Tc^{97}T = 10^4$ years), which made possible the isolation of weighable quantities of this element.

There is a great deal of interest in the chemical properties of element number 85, astatine, the heavy analog of the halogen group. This element, while remaining close in its properties to those of its nearest analog, iodine, differs considerably from it in that it is not a typical non-metal. In agreement with the general laws of the periodic system, basic properties are also manifested in astatine. Thus, for example, astatine is precipitated by hydrogen sulfide from acid solutions, and is evolved at the cathode upon electrolysis.

The use of artificial radioactive elements has opened completely new prospectives for chemistry in relation to one of its basic questions – the study of the chemical bond. Radioactive methods make possible the easy distinguishing of radioactive isotopes of a given element from each other and from inactive isotopes; therefore, through

the use of radioactive elements (by the so-called "marked" atom method) it is possible to trace the process of movement of the same kind of atom from one molecule to another or between different positions in the same molecule. The study of the kinetics of such changes makes possible the obtaining of data on the mobility of atoms linked in the molecule in various ways. Thus, for example, A. A. Greenberg and co-workers studied the speed of exchange of central and peripheral atoms in various inorganic complex salts, and showed that exchange of peripheral atoms takes place quite quickly even in such stable complex salts as bromoplatinates and bromoplatinites, but that exchange of central atoms in complex compounds is practically absent.

Artificial radioactive elements have been widely used for the study of the equivalence of bonds in complex compounds (A. E. Polesitsky, Ya. A. Fialkov, Yu. P. Nazarenko), the mobility of halogen atoms in various organic compounds (the first work in this direction was done by S. Z. Roginsky and co-workers), etc. The use of artificial radioactive isotopes for the study of the mechanism of chemical reactions has proved very fruitful.

The use of artificial radioactivity has opened up great possibilities in analytical chemistry. The possibility of simple and easily determining radioactive elements in the presence of extraneous non-radioactive substances has made possible the study of the rate and degree of completenes of analytical separations. After adding very small quantities of its radioactive isotope to the element to be determined, it is possible to check its loss in all stages of analysis through its radioactivity and to make corrections in its quantity, if necessary. This use of radioactive isotopes as an indicator for the control of the degree of completeness of separation during complex analyses was first proposed by I. E. Starik in connection with the determination of the content of lead in its ores and is today widely used in analytical chemistry.

The phenomena of artificial radioactivity are also successfully used directly for the determination of very small quantities of many elements. This use, so-called activation analysis, is based on the fact that the probability of neutron capture during the formation of radioactive isotopes varies greatly from element to element ($10^4 - 10^5$ times); therefore, by bombarding any element which is difficult to activate with a powerful neutron source and measuring the radioactivity which is obtained as a result, it is possible to determine very small quantities of strongly activated admixtures. The sensitivity and selectivity of activation analysis can be raised still more by means of the chemical separation of the radioactive elements which are formed after the addition of their inactive isotopes as carriers, and also by the correct selection of the length of bombardment and of the time lag between bombardment and the taking of measurements. Activation analysis makes possible the determination, for example, of $6 \cdot 10^{-9}$ g of manganese, $7 \cdot 10^{-9}$ g of sodium and gallium, $2 \cdot 10^{-9}$ g of scandium and arsenic, $3 \cdot 10^{-10}$ g of lanthanum, and $3 \cdot 10^{-11}$ g of europium and dysprosium. It has found practical use in America in the control of the chemical purity of germanium for radio-technical purposes, when the quantity of a number of admixtures must not rise above 10^{-6}%.

The use of artificial radioactive isotopes has proved very valuable in the analysis of complex mixtures of compounds which are difficult to separate; the method is called "isotope dilution". This method is based on the fact that different isotopes of the same element (with the exception of the hydrogen isotopes) are not separated from each other in ordinary chemical operations. Let us now introduce into the mixture to be analyzed, a mixture of amino acids obtained on hydrolysis of some protein for example, a certain quantity of one of the amino acids marked with the radioactive carbon isotope C^{14}, the specific activity of which (activity per mg) is known. After careful mixing the marked molecules are distributed equally among all the molecules of the given amino acid, and this distribution does not undergo any further change in the process of analysis; therefore, it is sufficient to separate an arbitrary part of the amino acid in the pure form and determine its specific activity in order to calculate the quantity of the given amino acid in the mixture, since the change in the specific activity is determined by the relationship between the amount of the amino acid which was added and the amount of it originally found in the mixture. This makes the quantative separation of the mixture unnecessary. The use of radioactive methods allowed A. L. Kursanov and his students to achieve important successes in the study of the processes of plant nutrition. They were able to prove that plants can assimilate carbon dioxide not only from atmospheric air through their leaves, but also through the root system from the air in the soil. They also succeeded in tracing further the course of synthesis of hydrocarbons and proteins from carbon dioxide in the plant. These results considerably deepened and broadened our knowledge of plant physiology, and will undoubtedly aid Soviet agro-biologists in the struggle to increase productivity, and for the creation of an abundance of agricultural products.

The examples which we have given far from exhaust all the uses of artificial radioactive isotopes in chemistry. In metallurgy, biology, medicine and electro-chemistry, the uses of radioactive methods, which were

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REACTIONS BETWEEN ZIRCONIUM NITRATE AND THE IODATES OF THE ALKALI METALS IN SOLUTIONS

III. THE INFLUENCE OF THE ALKALI METALS ON THE COMPOSITION OF ZIRCONIUM IODATE AND ON REACTIONS IN WHICH PRECIPITATES ARE FORMED

M. I. Konarev and A. S. Solovkin

Earlier [1, 2], it was shown that zirconium hydroxyiodate was precipitated out when potassium iodate was added to a solution of zirconium nitrate. The precipitates had the following compositions: $Zr(OH)_3IO_3 \cdot 4H_2O$ and $ZrOH(IO_3)_3 \cdot 4H_2O$.

Upon long standing with mother liquors containing potassium iodate, hydroxyiodates which were amorphous in form, are crystallized, being transformed thereby into the hexaiodate – $Zr(IO_3)_4 \cdot 2KIO_3$, and the enaiodate – $Zr(IO_3)_4 \cdot 3KIO_3 \cdot 2HIO_3$. Ordinarily, a mixture is formed with varying contents of the hexa- and enaiodate. The composition of the mixture depends on the concentration of potassium iodate in the solution and on the acidity.

1. The Influence of the Concentration of the Hydrogen Ion and the Ions of Certain Alkali Metals on the Composition of the Zirconium Iodate Precipitate

The results described below were obtained with the utilization of iodic acid and the iodates of sodium, lithium, and rubidium as precipitating agents.

The quantity of zirconium in the original solution was equal to 1.386 g/l, and its content in the precipitate corresponded to 0.693 g/l or 0.0076 g-ion/l. Under these conditions, we obtained a zirconium iodate precipitate when potassium iodate was used. The preparation of the samples and their analysis were carried out by the methods described earlier [1].

The results obtained with iodic acid are given in Table 1, with sodium iodate – in Table 2, with lithium iodate – in Table 3, and with rubidium iodate – in Table 4. In these tables, only the composition of the precipitates which had settled from the solution for a long time is given, since the composition of the precipitating agent does not influence that of the freshly precipitated zirconium iodate.

On the addition of iodic acid, or of the iodates of the alkali metals (sodium, lithium, or rubidium) to a zirconium nitrate solution, hydroxyiodates are precipitated, as in the case of the addition of potassium iodate. From nitric acid solutions with a sufficiently high concentration of the precipitating agent, zirconium triiodate settles out. The form of the precipitate changes depending on the precipitating agent that is used. A more powdery residue is formed when potassium or rubidium iodate is used than when iodic acid or the iodates of sodium and lithium are employed as precipitants.

Iodic acid has a special significance in relation to the iodates of the alkali metals. Very concentrated solutions of these iodates may be prepared from iodic acid, while the solubility of the iodates of the alkali metals in water and in nitric acid is limited. If concentrated iodic acid is added to a solution of zirconium nitrate, at first a precipitate is formed; but when the concentration of iodic acid reaches approximately 0.75 M, the precipitate is fully dissolved. A further increase in the concentration of iodic acid stabilizes the solution.

Solutions of zirconium iodate in iodic acid are, evidently, colloidal in nature, since upon the addition of a small amount of a salt (potassium, ammonium, or aluminum nitrate), zirconium is precipitated in the form of a triiodate of the same composition as before its dissolution in iodic acid.

Upon long standing of triiodates with moderately concentrated solutions of iodic acid, and also with solutions of sodium, lithium, or rubidium iodates, the crystallization of the precipitate takes place; the same is true of solutions containing potassium iodate. The crystallization of zirconium iodate takes place more slowly in the presence of iodic acid and the iodates of sodium and lithium than it does in the presence of potassium and rubidium iodates. The precipitate is crystallized most quickly in the presence of rubidium iodate.

TABLE 1

Precipitating agent – iodic acid

Experiment No.	Concentration of HIO_3 in the solution (in moles/l)	Found in the precipitate (in %)			Ratio Zr : IO_3	Ratio of K : Zr : IO_3 with the same molecular concentrations of KIO_3
		Zr	IO_3	Sum		
		0.02 N HNO_3				
1	0.026	22.00	47.92	69.92	1 : 1.13	Not determined
2	0.068	17.36	62.03	79.39	1 : 1.89	0.16 : 1 : 1.60
3	0.103	11.50	82.54	94.04	1 : 3.74	0.49 : 1 : 2.35
4	0.164	11.42	84.20	95.62	1 : 3.84	0.61 : 1 : 2.51
5	0.294	11.11	84.12	95.23	1 : 3.94	Solution KIO_3 is lower.
6	0.476	The original precipitate has been fully dissolved.				
		0.5 N HNO_3				
7	0.053	10.69	81.10	91.79	1 : 3.97	1.49 : 1 : 5.34
8	0.109	11.42	80.73	92.15	1 : 3.70	2.06 : 1 : 6.81
9	0.200	11.97	80.25	92.22	1 : 3.49	2.6 : 1 : 8.0
10	0.501	10.71	85.32	96.03	1 : 4.11	Solution KIO_3 is lower.
		1.75 N HNO_3				
11	0.038	11.17	74.81	85.98	1 : 3.72	Not determined
12	0.090	12.07	79.23	91.30	1 : 3.42	1.93 : 1 : 5.86
13	0.180	11.32	80.28	91.60	1 : 3.69	2.43 : 1 : 7.85
14	0.311	11.28	82.68	93.96	1 : 3.81	2.57 : 1 : 8.07
15	0.584	11.24	84.63	95.87	1 : 3.94	Solution KIO_3 is lower.

TABLE 2

Precipitating agent – sodium iodate; acidity of the solution on HNO_3 0.5 N

Experiment No.	Concentration of $NaIO_3$ in the solution (in moles /l)	Found in the precipitate (in %)				Ratio Na: Zr : IO_3	Ratio of K : Zr : IO_3 with the same molecular concentrations of KIO_3
		Na	Zr	IO_3	Sum		
1	0.029	–	10.91	79.46	90.37	0 : 1 : 3.90	Not determined
2	0.097	–	10.62	80.86	91.48	0 : 1 : 3.96	2.08 : 1 : 6.69
3	0.157	–	12.01	78.04	90.05	0 : 1 : 3.41	2.50 : 1 : 7.62
4	0.244	0.70	10.02	82.65	93.77	0.28 : 1 : 4.29	2.59 : 1 : 7.97
5	0.484	3.88	7.14	87.38	98.40	2.15 : 1 : 6.39	Not determined

TABLE 3

Precipitant – lithium iodate; acidity of the solution on HNO_3 0.53 N

Experiment No.	Concentration of $LiIO_3$ in the solution (in moles/l)	Found in the precipitate (in %)				Ratio Li : Zr : IO_3	Ratio of K : Zr : IO_3 with the same molecular concentrations of KIO_3
		Li	Zr	IO_3	Sum		
1	0.049	–	10.27	79.00	89.27	0 : 1 : 4.00	
2	0.092	–	10.45	77.10	87.55	0 : 1 : 3.84	2.08 : 1 : 6.72
3	0.192	–	11.31	75.78	87.09	0 : 1 : 3.51	2.50 : 1 : 7.62•
4	0.287	0.8	8.97	75.88	85.65	0.25 : 1 : 4.45	2.59 : 1 : 7.97••
5	0.490	5.2	7.42	89.22	101.84	2.02 : 1 : 6.25	Not determined

• With 0.161 N on KIO_3.

•• With 0.241 N on KIO_3.

TABLE 4

Precipitating agent – rubidium iodate; acidity of the solution on HNO_3 0.54 N

Experiment No.	Concentration of $RbIO_3$ in the solution (in moles/l)	Found in the precipitate (in %)				Ratio Rb : Zr : IO_3	Ratio of K : Zr : IO_3 with the same molecular concentrations of KIO_3
		Rb	Zr	IO_3	Sum		
1	0.061	13.16	7.01	81.45	101.62	1.99 : 1 : 6.05	1.77 : 1 : 5.65
2	0.078	12.90	6.73	81.50	101.13	2.06 : 1 : 6.31	2.02 : 1 : 5.98
3	0.096	12.96	6.28	82.34	101.58	2.19 : 1 : 6.83	2.08 : 1 : 6.72

It is apparent from a comparison of the data in Tables 1-4 that the composition of the precipitant not only influences the speed of crystallization of the precipitates, but also their final composition.

Upon long standing with a solution of iodic acid (Table 1), zirconium triiodate is converted into the tetraiodate, and not into the hexa- or enaiodate, as with potassium iodate.

Different quantities of the triiodate were converted into the tetraiodate after being allowed to stand for the same length of time (about 1 month) with iodic acid solutions of various concentrations. The reaction goes more completely with low or high concentrations of iodic acid in the solution (Experiments 7, 11, 5, 10 and 15, Table 1). The reasons for the incomplete conversion of the triiodate into the tetraiodate with moderate concentrations of iodic acid in the solution have not been explained.

In a 0.02 N nitric acid solution, with the concentration of iodic acid equal to 0.026 M, the replacement of the hydroxyl groups in the monoiodate by iodate groups is made more difficult as a result of hydrolysis (experiment 1, Table 1). Water of crystallization, as well as hydroxyl groups, made up part of the composition of the hydroxyiodates which were dried in the air; as a result of this the total content of zirconium and of the iodate groups in the precipitate is less than 100%. Two molecules of water of crystallization apparently enter into the composition of zirconium tetraiodate (experiments 5, 10 and 15, Table 1); however, its content in the tetraiodate precipitate has not been definitely determined.

Upon long standing of zirconium triiodate with mother liquors which contain sodium or lithium iodate, the triiodate may be converted into a mixture of the precipitates of the hexa- and enaiodates. The formation of the hexa- and enaiodate takes place only at high concentrations close to saturation with the corresponding iodate (experiment 5, Tables 2 and 3). At lower concentrations of $LiIO_3$ or $NaIO_3$, the behavior of the precipitate is similar to that observed in the experiments with iodic acid. With rubidium, the most stable complex zirconium-iodic acid compounds are formed; therefore, in order to obtain a precipitate of the same concentration as with potassium iodate, a smaller molecular concentration of rubidium iodate in solution is required (Table 4).

On the conversion of hydroxyiodates into complex compounds, the dehydration of the precipitate takes place. According to the analytical data, the total content of the alkali metal, zirconium, and the iodate groups is often somewhat more than 100%; this is probably due to errors in the carrying out of the analysis.

Thus, when the precipitates of zirconium hydroxyiodates are allowed to stand for a long time with solutions containing iodates of the alkali metals, complex compounds of the double salt type of the following composition are formed:

$$Zr(IO_3)_4 \cdot 2MeIO_3 \text{ and } Zr(IO_3)_4 \cdot 3MeIO_3 \cdot 2HIO_3,$$

(Me equals potassium, sodium, lithium, or rubidium).

The stability of the complex iodic acid compounds of zirconium rises with a change in the composition of the precipitant in the following order:

$$LiIO_3,\ NaIO_3,\ KIO_3,\ RbIO_3.$$

With iodic acid, tetraiodates are formed.

2. Reactions in Which Zirconium Hydroxyiodates are Formed.

Many experiments showed that the composition of the precipitate of zirconium iodate depends to a considerable extent on the composition of the zirconium nitrate in solution. Together with this, the concentration of the iodate ion also has an important influence, especially when the precipitation takes place from solutions of

increased acidity. The formation of hydroxyiodates is characteristic of zirconium; it is impossible to explain this phenomenon by the properties of zirconium iodate alone. This is graphically illustrated by the results given in Table 5.

When zirconium is precipitated from an aqueous solution of its nitrate (pH 2-3), that is, under conditions of the greatest possible hydrolysis of zirconium nitrate, only the monoiodate appears in the precipitate regardless of the concentration of the iodate ion in the solution (experiment 1, Table 5). The influence of the hydrolysis of zirconium nitrate on the composition of the iodate precipitate is also considerable in a 0.07 N nitric acid solution. On the precipitation of zirconium from such a solution too, the monoiodate is obtained, but in addition, precipitates are also formed which contain more than one iodate group for each zirconium atom (experiments 2,7, and 12, Table 5).

Precipitates which contain one iodate group for each zirconium atom can also be obtained from concentrated nitric acid solutions. In particular, zirconium was isolated in small quantities (in relation to the total content in the solution) in the form of the monoiodate from a 5 N nitric acid solution (experiments 2-5, Table 5).

On the precipitation of zirconium, the gradual formation of the precipitates is observed. This is graphically shown by the results of experiments carried out with 0.5 N and more concentrated nitric acid solutions. With an increase in the concentration of iodate ions in solution, there was an increase not only in the completeness of precipitation, but also in the number of iodate groups in the precipitate in relation to the zirconium content. The final product of the reactions in the solution is zirconium triiodate (experiments 12-15, Table 5).

TABLE 5

Dependence of the composition of zirconium hydroxyiodate on the concentration of iodate ions in solution and the acidity. Concentration of zirconium 0.0076 g-ion/liter

Experiment No.	Concentration of HNO_3 (normality)	Concentration of IO_3 in solution (in g-ion/l)	Ratio of IO_3/Zr in precipitate	Composition of the precipitate
		Zirconium monoiodate		
1	0.02	0.0097-0.161		
2	0.07	0.008		
3	0.5	0.011	1.0-1.3	$Zr(OH)_3IO_3 \cdot 4H_2O$
4	0.99	0.015		
5	5.0	0.037		
		Precipitates containing less than 3 iodate groups		
6	0.02	Not formed		
7	0.07	0.01-0.14		
8	0.5	0.015-0.06	$> 1 < 3$	Variable
9	0.99	0.02-0.06		
10	5.0	0.05-0.06		
		Zirconium triiodate		
11	0.02	Not formed		
12	0.07	0.152		
13	0.5	0.060-0.3	3.0-3.2	$ZrOH(IO_3)_3 \cdot 4H_2O$
14	0.99	0.060-0.35		
15	5.0	0.060-0.57		

The results obtained on fractional precipitation show that zirconium is precipitated when the nitrate groups are fully replaced by iodate groups; therefore, that part of the zirconium which is found in solution in the form of the mononitrate is precipitated, in the first place, in the form of the monoiodate; that part contained in the form of the dinitrate forms the diiodate; and zirconium trinitrate precipitates out in the form of zirconium triiodate.

Considering the process as a reaction between ions, the formation of zirconium hydroxyiodates may be represented by the following scheme:

Monoiodate $Zr(OH)_3^+ + IO_3^- \rightarrow Zr(OH)_3IO_3$,

Diiodate $Zr(OH)_2^{+2} + 2IO_3^- \rightarrow Zr(OH)_2(IO_3)_2$,

Triiodate $ZrOH^{+3} + 3IO_3^- \rightarrow ZrOH(IO_3)_3$.

TABLE 6

Composition of the amorphous and crystalline phases of precipitates isolated before the establishment of equilibrium

Experiment No.	Concentration of HNO_3 (normality)	Ratio of K : Zr : IO_3 according to analysis	
		amorphous	crystalline
1	0.02	0 : 1 : 1.12	1.99 : 1 : 6.04
2		0 : 1 : 1.15	2.02 : 1 : 6.15
3	0.48	0 : 1 : 2.98	2.06 : 1 : 6.17
4		0 : 1 : 3.07	2.06 : 1 : 6.28

TABLE 7

Influence of the relative concentrations of iodic acid and potassium iodate on the composition of the zirconium iodate precipitate

Experiment No.	Concentration of IO_3 (in moles/l)		Numerical value of the ratio of the molecular concentrations of $HIO_3 : KIO_3$	Numerical value of the ratio IO_3 : Zr in the precipitate.
	total	in KIO_3		
1	0.294	None	–	3.94
2	0.283	0.035	7.10	8.51
3	0.284	0.118	1.40	8.90
4	0.291	0.207	0.41	8.00
5	0.304	0.056	4.40	9.06
6	0.303	0.219	0.38	8.23
7	0.310	0.248	0.25	7.93
8	0.501	None	–	4.11
9	0.437	0.066	5.62	8.23

TABLE 8

Influence of the acidity of the solution on the composition of the zirconium iodate precipitate

Experiment No.	Concentration of HNO_3 (normality)	Concentration of KIO_3 (in moles/l)	Numerical value of the ratio in the precipitate	
			IO_3 : Zr	IO_3 : K
1	0.18	0.094	7.03	3.04
2	0.48	0.095	6.72	3.18
3	0.98	0.091	6.10	2.96
4	1.75	0.090	6.08	2.99
5	3.3	0.094	5.46	5.44
6	4.2	0.090	5.69	4.83
7	0.18	0.156	7.94	3.06
8	0.48	0.161	7.62	3.04
9	0.98	0.167	7.23	3.16
10	1.75	0.155	7.32	3.22
11	3.3	0.168	6.57	3.85
12	4.2	0.156	6.24	3.77

The presence of the $Zr(OH)_3^+$ and $Zr(OH)_2^{+2}$ ions in the nitric acid solutions may be shown by the fractional precipitation of zirconium (at low concentrations of iodate ions in solution). On the addition of a large excess of dissolved iodate to the nitric acid solution, zirconium triiodate is precipitated. If the concentration of iodate ions is increased in a solution from which part of the zirconium has already been precipitated out in the form of the monoiodate or of a mixture with an average content of less than three iodate groups for each zirconium atom, the precipitate is converted into the triiodate.

TABLE 9

The influence of the concentration of the dissolved potassium found in solution on the composition of the zirconium iodate precipitate

Experiment No.	Concentration in the solution (in moles/l)			Numerical value of the ratio in the precipitate		
	HNO_3	IO_3	K	K : Zr	IO_3 : Zr	IO_3 : K
1	3.3	0.133	0.133	1.35	5.89	4.36
2		0.122	0.567	1.85	6.22	3.36
3		0.168	0.168	1.70	6.57	3.87
4		0.160	0.605	2.18	6.71	3.08
5		0.193	0.193	2.03	6.99	3.34
6		0.216	0.681	2.34	7.19	3.07
7	4.2	0.160	0.160	1.65	6.28	3.81
8		0.181	0.626	2.07	6.34	3.06

On the basis of these results, it is evident that the monoiodate and the diiodate, on contact with the mother liquor, can be converted into the triiodate.

Such a conversion can be represented in the following way:

$$Zr(OH)_3IO_3 + 2H^+ + 2IO_3^- \rightarrow ZrOH(IO_3)_3 + 2H_2O,$$

$$Zr(OH)_2(IO_3)_2 + H^+ + IO_3^- \rightarrow ZrOH(IO_3)_3 + H_2O.$$

For 0.5 N and more concentrated nitric acid solutions, the concentration of the iodate ion has more significance than the acidity: therefore, in order to obtain zirconium triiodate, both from 0.5 N and 5 N nitric acid solutions, approximately the same concentration (about 0.06 g-ion/l) of the iodate ion is required (experiments 13-15, Table 5).

The results of a study of the reaction in which zirconium iodate is formed did not confirm the existence of the zirconyl ion in the nitric acid solution. If zirconium were present in the form of the zirconyl ion, zirconyl iodate would probably be formed. This, however, was not observed in any of the experiments carried out with nitric acid solutions of various concentrations (from 0.02 to 7.5 N). In 0.5 N and more concentrated nitric acid solutions, the greater part of the zirconium was found in the form of $ZrOH^{+3}$. In addition, even in a 5 N solution of nitric acid, the $Zr(OH)_3^+$ ion was found, which creates a basis for supposing the existence of the $Zr(OH)_2^{+2}$ ion.

3. Reactions in Which Zirconium Hexa- and Enaiodates are Formed.

The results of the experiments carried out with mixtures of iodic acid and potassium iodate, and with nitric acid solutions containing potassium iodate were used for the examination of these reactions.

The relatively high solubility of potassium iodate in iodic and nitric acid solutions made possible the carrying out of experiments over wide intervals of concentration of the iodate and potassium ions; the comparatively high stability of potassium-zirconium-iodic acid salts made the obtaining of these compounds possible with small concentrations of potassium iodate in solution.

The composition of the precipitates which are formed on the use of potassium iodate on long standing with mother liquors has been examined in detail earlier (2). In the present article this data is supplemented by the results of the analysis of amorphous and crystalline precipitates which separate out before a state of equilibrium had been reached between the solid and liquid phases; data is also given showing the influence of the addition of potassium nitrate on the composition of the precipitates.

The results of the determination of the composition of the amorphous and crystalline phases are given in Table 6. The separation was carried out by the decantation in the mother liquor of the slowly settling amorphous precipitate from the quickly settling crystalline precipitate.

In Table 7 data is given on the composition of zirconium iodate precipitates obtained with changing ratios of the molecular concentrations of iodic acid and potassium iodate, and with a constant concentration of nitric acid in solution equal to 0.02 N. The data of Table 7 show the changes in the quantity of the enaiodate formed with the indicated changes in the composition of the liquid phase.

In Table 8 data is given characterizing the influence of the concentration of nitric acid on the composition of the zirconium iodate precipitate, and in Table 9, the data showing the influence of the concentration of the potassium ion, the concentration of nitric acid remaining constant.

In examining the reaction of the formation of the hexa- and enaiodates, it is necessary to keep in mind that the composition of the final product varies with the nature of the precipitant used. The reaction of the freshly-precipitated hydroxyiodate with the iodic acid contained in the solution is completed with the formation of the tetraiodate. The same final composition is also observed with moderate concentrations of sodium or lithium iodate in the solution.

When the monoiodate is present in the precipitate, three hydroxy groups are replaced by iodate groups. in the hydroxydiiodate, two hydroxy groups are replaced by iodate groups, and in the hydroxytriiodate, one hydroxy group is replaced by an iodate group:

$$Zr(OH)_3IO_3 + 3H^+ + 3IO_3^- \rightarrow Zr(IO_3)_4 + 3H_2O,$$

$$Zr(OH)_2(IO_3)_2 + 2H^+ + 2IO_3^- \rightarrow Zr(IO_3)_4 + 2H_2O,$$

$$Zr(OH)(IO_3)_3 + H^+ + IO_3^- \rightarrow Zr(IO_3)_4 + H_2O.$$

The zirconium tetraiodate which is formed is stable in the presence of iodic acid solutions. When the ions of the alkali metals are present, especially those of potassium and rubidium, the tetraiodate is converted into the hexa- or the enaiodate. If, on the interaction of the precipitate with the solution, the amorphous phase is separated from the crystalline phase, this indicates that the first corresponds in composition to the freshly-precipitated hydroxyiodate, and the second corresponds to the precipitate of the equilibrium phase (Table 6).

The quantity of hexa- and enaiodates which is formed in their mixtures depends on both the total concentration of iodate ions in the solution, and on the ratio of the moelcular concentrations of iodic acid and potassium iodate. With a concentration of iodic acid sufficiently high to prevent the hydrolysis of zirconium iodate, a small concentration of potassium iodate in the solution is necessary for the formation of the hexaiodate. A considerable increase in the concentration of potassium iodate in the solution also does not influence the full conversion of the precipitate into the hexaiodate (Table 7). These, and other experiments show that for the conversion of the triiodate, the relative concentration of iodic acid and potassium iodate is not significant. The only important factors are sufficiently high concentrations of potassium iodate and the hydrogen ion (the raising of the acidity of the solution is necessary to prevent hydrolysis of the zirconium iodate precipitate).

Taking into consideration the conditions of the formation of the hexaiodate, the following scheme is the most reliable representation of its formation:

$$ZrOH(IO_3)_3 + H^+ + IO_3^- + 2KIO_3 \rightarrow Zr(IO_3)_4 \cdot 2KIO_3 + H_2O.$$

For the conversion of the entire precipitate into the enaiodate, the composition of the mother liquor has essential significance. It is necessary that the mother liquor have a high concentration of iodic acid and a relatively low concentration of potassium iodate. With high concentrations of iodic acid and relatively low concentrations of potassium iodate in the solution, the formation of the double salt $KIO_3 \cdot 2HIO_3$ is observed; this salt was studied in detail by Meerburg in 1905 (3].

Starting from the composition of the enaiodate, and from the conditions under which it can be obtained, and taking into consideration the data of the investigation of the system $HIO_3 - KIO_3$ [3], the following scheme is the most probable one for the conversion of the precipitate into the enaiodate:

$$ZrOH(IO_3)_3 + H^+ + IO_3^- + 2KIO_3 + KIO_3 \cdot 2HIO_3 \rightarrow Zr(IO_3)_4 \cdot 3KIO_3 \cdot 2HIO_3 + H_2O.$$

The $KIO_3 \cdot 2HIO_3$ molecules can probably be formed, not only with high concentrations of iodic acid and low concentrations of potassium iodate, but also in these conditions when there is a sufficiently high concentration of the hydrogen, iodate, and potassium ions in the solution. This is evidently the explanation of the ability of zirconium triiodate to form (usually) mixtures of hexaiodate and enaiodate on long standing with the mother liquors.

The formation of the enaiodate takes place, not only on the precipitation of zirconium by a mixture of iodic acid and potassium iodate, but also under those conditions when potassium iodate dissolved in dilute nitric

acid or water, is used as a precipitant (with precipitation by potassium iodate dissolved in water, it is necessary to use a nitric acid solution of zirconium nitrate).

When potassium iodate is used, the greatest quantity of the enaiodate is found in the mixture when the mother liquors are saturated with KIO_3; under these conditions, even with an increase in the concentration of the nitric acid, the solubility of the potassium iodate is increased, and the average composition of the mixture of precipitates settling out of 0.18, 0.48, 0.98, 1.75, 4.2, 5.0 and 7.5 N nitric acid solutions turns out to be approximately the same, with the ratio of $Zr : IO_3 = \sim 1 : 8$. With the utilization of a 3.3 N nitric acid solution, saturated with potassium iodate, precipitates with an average content of about 8.6 iodate groups to one zirconium atom were obtained [2]. The last experiment showed that within the limits of 2-4 N nitric acid, saturated with potassium iodate, more favorable conditions are created for the formation of the complex molecules $KIO_3 \cdot 2HIO_3$, than in less concentrated nitric acid solutions.

The high acidity of the solution influences the composition of the precipitates formed with concentrated nitric acid solutions. The formation of acid salts is possible on contact between zirconium iodate and nitric acid solutions; this is disclosed by changes in the numerical value of the ratio between the iodate groups and the potassium in the precipitate. In the normal salts the numerical value of the ratio between the iodate groups and potassium is equal to 3, while in the acid salts it is greater than 3 (Table 9).

Even with the partial replacement of the potassium by the hydrogen ion, the stability of the complex compound is lowered, as a consequence of which the quantity of the enaiodate in the mixture decreases.

With an increase in the concentration of the potassium ion as a result of the introduction of potassium nitrate in a nitric acid solution, the equilibrium is shifted in the direction of the formation of the normal salts; together with this, the quantity of the enaiodate in the precipitate is increased. (experiments 2, 4, 6, and 8, Table 9). The shifting of the equilibrium in the direction indicated is in conformity with the general principle of such changes, since on the addition of potassium nitrate the dissociation of nitric acid is lowered, and the concentration of potassium entering into the composition of the precipitate is increased.

With the use of $LiIO_3$, $NaIO_3$ and $RbIO_3$ as the precipitant, the same conformity with the general principle is observed as in the case of potassium iodate, but when these precipitants are used the individual properties of a given alkali metal also influence the course of the reaction.

SUMMARY

1. The composition of freshly-precipitated zirconium iodate was determined by the extent of the hydrolysis of its nitrate in solution, and also by the concentration of iodate ions.

At a pH of 2-3, zirconium is found in the form of $Zr(OH)_3^+$; therefore, on the addition of the dissolved iodate, the monoiodate is formed. In 0.07 N and more concentrated nitric acid solutions, zirconium forms three types of ions: $Zr(OH)_3^+$, $Zr(OH)_2^{+2}$ and $ZrOH^{+3}$. On the fractional precipitation of zirconium with small portions of the dissolved iodate, the corresponding hydroxyiodates are precipitated:

$$Zr(OH)_3IO_3 \cdot 4H_2O,\ Zr(OH)_2(IO_3)_2 \cdot 4H_2O \text{ and } ZrOH(IO_3)_3 \cdot 4H_2O.$$

Precipitates of two compositions were isolated – the monoiodate and the triiodate. The monoiodate and the diiodate are converted into the triiodate when high concentrations of the iodate ion are present in solution. The zirconyl ion was not detected in the nitric acid solutions.

2. Upon long standing with a mother liquor containing iodic acid, zirconium triiodate is converted into the tetraiodate.

In the presence of the iodates of the alkali metals, the triiodate is converted into the hexa- and the enaiodate.

In solutions of high acidity, the acid salt $Zr(IO_3)_4 \cdot MeIO_3 \cdot HIO_3$, is formed along with the normal salt.

3. The stability of the iodic acid complexes of zirconium compounds increases with the use of precipitants in the following order: $LiIO_3$, $NaIO_3$, KIO_3, $RbIO_3$.

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THE SOLUBILITY PRODUCTS OF THE OXALATES OF SOME RARE-EARTH ELEMENTS AND THE DISSOCIATION CONSTANTS OF THEIR COMPLEX SULFATES

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There is very little data in the literature on the solubility products of the oxalates of the rare-earth elements. It is most often mentioned that the solubility product of lanthanum oxalate is equal to $2 \cdot 10^{-28}$ at 18° [1-4]. The value for the solubility product of cerium oxalate according to some data is equal to $2.5 \cdot 10^{-29}$ at 25° [3,4], and for the oxalate of neodymium or praseodymium a value of $5.9 \cdot 10^{-29}$ at 25° is given in [4]. The solubility in water at 25° of the oxalates in which we are interested is given in some works [5]; this data served as the basis for the calculation of the solubility products given above. These results were obtained by the determination of the electroconductivity of saturated solutions. However, according to Semenchenko [6], the method of electroconductivity is not devoid of errors. In addition, the oxalates of the rare-earth elements in their saturated solutions undergo hydrolysis to a certain extent as a consequence of which the results of determinations carried out by this method may be low. Some investigators [7, 8] determine the solubility of the rare-earth elements in sulfuric acid. But the results of the data are insufficient for the calculation of the solubility products; therefore we carried out a series of studies for the determination of the solubility products of the oxalates of lanthanum, cerium and praseodymium. The determination was carried out by the method used by Zharovsky [9] for the determination of the solubility products of phosphates.

We determined the solubility products of oxalates from their solubility in hydrochloric acid solutions of various concentrations. In order to obtain saturated solutions, the oxalate was agitated for three hours with a solution of hydrochloric acid of known concentration. Agitation for this length of time is sufficient to achieve saturation.

$$Me_2(C_2O_4)_3 + 6H^{\cdot} \rightarrow 2Me^{\cdot\cdot\cdot} + 3H_2C_2O_4. \quad (1)$$

We determined the pH, and the total concentration of the oxalate, s, in the solution obtained in this way; the concentration of the oxalate was determined by titration with permanganate in the presence of manganese sulfate. The concentration of the cation of the rare-earth element was calculated from the value of s that was found:

$$[Me^{\cdot\cdot\cdot}] = \frac{2}{3}s. \quad (2)$$

The total concentration of oxalic acid was obtained by adding the concentrations of its various forms, which had been titrated with permanganate:

$$s = [C_2O_4^{\cdot\cdot}] + [HC_2O_4^{\cdot}] + [H_2C_2O_4]. \quad (3)$$

The concentration of each form depends on the concentration of the hydrogen ion and on the dissociation constant of oxalic acid

$$[HC_2O_4^{\cdot}] = [C_2O_4^{\cdot\cdot}] \cdot \frac{[H^{\cdot}]}{k_2}, \quad (4)$$

$$[H_2C_2O_4] = [C_2O_4^{\cdot\cdot}] \cdot \frac{[H^{\cdot}]^2}{k_1 \cdot k_2}. \quad (5)$$

Thus, the concentration of $HC_2O_4^{\cdot}$ and $H_2C_2O_4$ can be expressed by the concentration of the $C_2O_4^{\cdot\cdot}$ ion and of the hydrogen ion.

Let us suppose that the total concentration of the oxalate is equal to 1 M; then

$$s = 1 = [C_2O_4^{\cdot\cdot}] + [HC_2O_4^{\cdot}] + [H_2C_2O_4]. \quad (6)$$

We shall substitute for the values of $HC_2O_4^{\cdot}$ and $H_2C_2O_4$ their values from equations (4) and (5):

$$s = 1 = [C_2O_4^{\cdot\cdot}] + [C_2O_4^{\cdot\cdot}] \cdot \frac{[H^{\cdot}]}{k_2} + [C_2O_4^{\cdot\cdot}] \cdot \frac{[H^{\cdot}]^2}{k_1 \cdot k_2}, \quad (7)$$

whence

$$s = 1 = [C_2O_4^{''}]\left(1 + \frac{[H^{\cdot}]}{k_2} + \frac{[H^{\cdot}]^2}{k_1 \cdot k_2}\right), \quad (8)$$

$$[C_2O_4^{''}] = \frac{k_1 \cdot k_2}{k_1 \cdot k_2 + k_1[H^{\cdot}] + [H^{\cdot}]^2} = \frac{3.96 \cdot 10^{-6}}{3.96 \cdot 10^{-6} + 6.5 \cdot 10^{-2}[H^{\cdot}] + [H^{\cdot}]^2}. \quad (9)$$

TABLE 1

Dependence of the concentration of $C_2O_4^{''}$ on the pH with $\underline{s} = 1$

pH	$[C_2O_4^{''}]$	$-\log [C_2O_4^{''}]$
0	$3.7 \cdot 10^{-6}$	5.43
0.5	$3.3 \cdot 10^{-5}$	4.48
1.0	$2.5 \cdot 10^{-4}$	3.60
1.5	$1.3 \cdot 10^{-3}$	2.89
2.0	$6.0 \cdot 10^{-3}$	2.22
2.5	$1.9 \cdot 10^{-2}$	1.72
3.0	$5.7 \cdot 10^{-2}$	1.25
4.0	$3.8 \cdot 10^{-1}$	0.42
5.0	$8.5 \cdot 10^{-1}$	0.07

Equation (9) makes possible the calculation of the concentration of $C_2O_4^{''}$ in relation to the pH, with s = 1 (Table 1).

To simplify calculations, the $\log [C_2O_4^{''}]$ is plotted against the pH in accordance with this data. Through the use of such a graph, it is possible easily to find the concentration of $C_2O_4^{''}$ for any value of pH. This concentration of $C_2O_4^{''}$ is multiplied by the value of $\underline{s}$ found by titration. The product shows the concentration of $C_2O_4^{''}$ in the final solution. Finally, we introduce the values obtained for $C_2O_4^{''}$ and $Me^{\cdots}$ in the formula

$$PS = [Me^{\cdots}]^2 \cdot [C_2O_4^{''}]^3 \cdot f^2_{Me^{\cdots}} \cdot f^3_{C_2O_4^{''}}. \quad (10)$$

We will give an example of the calculations. A saturated solution of lanthanum oxalate in 0.02 N hydrochloric acid was prepared. The concentration of oxalic acid in this solution was $s = 2.25 \cdot 10^{-4}$ M. Therefore, $[La^{\cdots}] = 2/3 \cdot 2.55 \cdot 10^{-4} = 1.5 \cdot 10^{-4}$ g-ion/l. The pH of the saturated solution was equal to 1.61. According to the data of Table 1, (or better, from a graph constructed from the data), we find that at this pH the negative logarithm of the concentration of $C_2O_4^{''}$ is equal to 2.7, from which $[C_2O_4^{''}] = 2 \cdot 10^{-3}$ g-ion/l with s = 1. For $s = 2.25 \cdot 10^{-4}$ the concentration of $C_2O_4^{''}$ is equal to:

$$[C_2O_4^{''}] = 2.25 \cdot 10^{-4} \cdot 2 \cdot 10^{-3} = 4.5 \cdot 10^{-7} \text{ g-ion/l}.$$

Since all the determinations were carried out in the presence of comparatively large quantities of an electrolyte (the acid), the activity coefficients of the ions were taken into account in the calculations. The values taken for these coefficients were those given by Lurye [3].

From this data, we will calculate the solubility products of lanthanum oxalate:

$$(1.5 \cdot 10^{-4})^2 (4.5 \cdot 10^{-7})^3 (0.42)^2 (0.68)^3 = 1.07 \cdot 10^{-28}.$$

It is possible to determine the solubility product in a somewhat different way. The concentration of the cation in a saturated solution of the oxalate of the rare-earth element in hydrochloric acid is determined gravimetrically. For this, a known quantity of a saturated solution is evaporated until dry, then evaporated with nitric acid, roasted, and the residue, which is the metal oxide, is weighed. Knowing in this way the concentration of the cation, it is possible to calculate the total concentration of the oxalate, which is 1.5 times greater than the concentration of the cation. On the basis of this data, and the value of the pH of the saturated solution, the concentration of the $C_2O_4^{''}$ ion is found. The further calculations are carried out in the same way as with the preceeding method.

TABLE 2

Determination of the solubility product of calcium oxalate

Run	Normality of HCl	pH of the saturated solution	$[Ca^{\cdot\cdot}]$ (g-ion/l)	$[C_2O_4^{''}]$ (g-ion/l)	f	Activity coefficient
1	0.2	0.92	$9.0 \cdot 10^{-3}$	$1.7 \cdot 10^{-6}$	0.38	$2.2 \cdot 10^{-9}$
2	0.1	1.23	$4.4 \cdot 10^{-3}$	$2.5 \cdot 10^{-6}$	0.45	$1.8 \cdot 10^{-9}$
3	0.2	0.92	$1.1 \cdot 10^{-2}$	$2.2 \cdot 10^{-6}$	0.38	$3.5 \cdot 10^{-9}$
4	0.1	1.23	$5.1 \cdot 10^{-3}$	$2.8 \cdot 10^{-6}$	0.45	$2.3 \cdot 10^{-9}$
					Average	$2.5 \cdot 10^{-9}$

In order to verify the accuracy of the described method for the determination of the solubility products of oxalates, we first determined the solubility product of calcium oxalate at 20°. Calcium oxalate was selected by us because its solubility product has been determined many times and its value is well known. According to various data, this value is between $1.8 \cdot 10^{-9}$ [1-4] and $3.8 \cdot 10^{-9}$ [10]. The results of our determinations* of the solubility product of calcium oxalate are given in Table 2.

The first two determinations were carried out by volumetric methods, the second two – by gravimetric methods.

These results indicate that the method used for the determination of the solubility product (activity coefficient) of oxalates is satisfactorily accurate. The data for the oxalates of lanthanum, cerium, and praseodymium obtained by this method are given in Table 3. Each value is the average of several determinations, which were in good agreement with each other. Thus, our results agree quite well with the literature data. Some of the differences can be explained by differences in temperature and in the methods of the determination of these values.

TABLE 3

Determination of the solubility products of the oxalates of lanthanum, cerium, and praseodymium at 20°

Compound	Normality of HCl	$[Me^{\cdots}]$ (g-ion/l)	Total concentration of oxalic acid (in M)	pH of the saturated solution	$[C_2O_4^{\cdot\cdot}]$ (g-ion/l)	$f_{C_2O_4^{\cdot\cdot}}$	$f_{Me^{\cdots}}$	Solubility product	Solubility of the oxalate (in mg/l)
Lanthanum oxalate	0.02	$1.5 \cdot 10^{-4}$	$2.25 \cdot 10^{-4}$	1.61	$4.5 \cdot 10^{-7}$	0.68	0.42	$1.07 \cdot 10^{-28}$	0.54
Cerium oxalate	0.10	$7.7 \cdot 10^{-4}$	$1.15 \cdot 10^{-3}$	1.05	$3.6 \cdot 10^{-7}$	0.46	0.2	$1.10 \cdot 10^{-28}$	0.54
Praseodymium oxalate	0.02	$1.2 \cdot 10^{-4}$	$1.8 \cdot 10^{-4}$	1.77	$5.6 \cdot 10^{-7}$	0.68	0.42	$1.3 \cdot 10^{-28}$	0.58

We noticed that the oxalates of the rare-earth elements were considerably more soluble in sulfuric acid than in hydrochloric acid. This can be explained by the fact that in the case of sulfuric acid, the process of solution is accompanied by the formation of complex sulfates. Complex sulfates of the rare-earth elements of various compositions are known. Compounds with the composition $Na_3[Me(SO_4)_3]$ were described many years ago by Brauner [7]. Compounds of the composition $Na[Me(SO_4)_2]$ [5] were also isolated. The $MeSO_4^{\cdot}$ ion [11] is stable in aqueous solutions. Dissociation constants have been determined for several of these ions. The dissociation constant of $LaSO_4^{\cdot}$, found by potentiometric means, is equal to $2.4 \cdot 10^{-4}$ [12]. The dissociation constant of $CeSO_4^{\cdot}$, determined by the ion exchange method, is equal to $1.6 \cdot 10^{-2}$ [13]. The large difference in these values for analogous compounds of two very similar elements indicates that one (or both) of the methods used for the determination was inaccurate.

The increase in the solubility of the oxalates of the rare-earth elements in sulfuric acid compared with their solubility in hydrochloric acid provides a basis for the calculation of the dissociation constants of the complex sulfates of these elements (solubility method). Let us assume that, on dissolution in sulfuric acid, the reaction takes place chiefly according to the following equation:

$$Me_2(C_2O_4)_3 + 6H^{\cdot} + 2SO_4^{\cdot\cdot} \rightleftharpoons 2MeSO_4^{\cdot} + 3H_2C_2O_4. \quad (11)$$

In order to calculate the equilibrium constant, we divide equation (12) by equation (13) raised to the third power and by the square of equation (14):

$$PS = [Me^{\cdots}]^2 [C_2O_4^{\cdot\cdot}]^3, \quad (12)$$

$$\frac{[H^{\cdot}]^6 [C_2O_4^{\cdot\cdot}]^3}{[H_2C_2O_4]^3} = k_1 \cdot k_2, \quad (13)$$

$$\frac{[Me^{\cdots}][SO_4^{\cdot\cdot}]}{[MeSO_4^{\cdot}]} = k. \quad (14)$$

Whence we obtain

$$\frac{[MeSO_4^{\cdot}]^2 [H_2C_2O_4]^3}{[H]^6 [SO_4^{\cdot\cdot}]^2} = \frac{PS}{(k_1 \cdot k_2)^3 k^2}. \quad (15)$$

* E. N. Kuzmina participated in the experimental part of our work.

Equation (15) represents the equilibrium constant of reaction (11). Hence we find that

$$k = \sqrt{\frac{PS\ [H^{\cdot}]^6 \cdot [SO_4^{\cdot\cdot}]^2}{(k_1 \cdot k_2)^3\ (MeSO_4^{\cdot})^2\ [H_2C_2O_4]^3}}.$$

We now write the equation in simpler form and introduce the activity coefficients for greater accuracy

$$k = \frac{\sqrt{PS}}{7.4 \cdot 10^{-5}} \cdot \frac{[H^{\cdot}]^3 \cdot f_1^3 \cdot [SO_4^{\cdot\cdot}] \cdot f_2}{[MeSO_4^{\cdot}] \cdot f_1 \sqrt{[H_2C_2O_4]^3}}; \qquad (16)$$

in equation (16) f_1 is the activity coefficient of the monovalent ions, and f_2 the activity coefficient of the bivalent ions.

A saturated solution of the oxalate of a rare-earth element in a hydrochloric acid solution of known concentration was prepared. The pH of this solution and the total concentration of the oxalate were determined (titration with permanganate) or the total concentration of the oxalate was determined (gravimetric method). On the basis of this data, the other values necessary for the calculation of the dissociation constant were determined.

1. Knowing the pH of the saturated solution, the value of $[H^{\cdot}] \cdot f$, is found by the use of the equation $pH = -\log [H^{\cdot}] \cdot f$.

2. Calculations from the results of the analysis of the saturated solution. 5 ml of a saturated solution of the oxalate of the rare-earth element was titrated using a microburet with a 0.02 N permanganate solution; the total concentration of the oxalic acid was determined from this data. If, on titration, after making deductions for the indicated error, we have 0.68 ml of a 0.02143 N permanganate solution, the total concentration of oxalic acid is equal to:

$$\frac{0.68 \cdot 0.02143}{5.2} = 1.46 \cdot 10^{-3}\ M$$

It follows from equation (11) that the total concentration of the rare-earth element in the solution is equal to 2/3 of the total concentration of the oxalate. If the total concentration of the rare-earth element in the saturated solution is determined by gravimetric means, the total concentration of the oxalate can be found by multiplying the value for the concentration of the rare-earth element by 3/2.

3. Calculation of the concentration of the undissociated molecules of oxalic acid. For the determination of the dissociation constant through the use of equation (16) it is necessary to know, not the total concentration of the oxalic acid, but the concentration of its undissociated molecules. The total concentration of oxalic acid in the solution, s, is obtained by adding the concentrations of its individual forms (equation 3). Replacing $[HC_2O_4^{\cdot}]$ and $[C_2O_4^{\cdot\cdot}]$ by their values obtained from the corresponding dissociation constants, we have

$$s = [H_2C_2O_4] + \frac{k_1\,[H_2C_2O_4]}{[H^{\cdot}]} + \frac{k_1 \cdot k_2\,[H_2C_2O_4]}{[H^{\cdot}]^2},$$

whence

$$s = [H_2C_2O_4] \cdot \left(1 + \frac{5.9 \cdot 10^{-2}}{[H^{\cdot}]} + \frac{3.8 \cdot 10^{-6}}{[H^{\cdot}]^2}\right).$$

If we assume that s = 1, then it is possible to calculate the concentration of the undissociated molecules of oxalic acid in relation to the pH of the solution:

pH	0	0.5	1.0	1.5	2.0	2.5	3.0
$-\log [H_2C_2O_4]$ with s = 1	0.03	0.07	0.20	0.46	0.84	1.30	1.80

In accordance with this data, the $-\log [H_2C_2O_4]$ is plotted against the pH of the solution. For example, when the pH of the solution is equal to 1.35, we find that $-\log [H_2C_2O_4]$ is equal to 0.37 or $\log [H_2C_2O_4] = 1.63$, whence $[H_2C_2O_4] = 4.27 \cdot 10^{-1}$ M, with s = 1. But the total concentration is not equal to 1, but to $1.46 \cdot 10^{-3}$ M in our example. Therefore the concentration of the undissociated molecules of oxalic acid is equal to $4.27 \cdot 10^{-1} \cdot 1.46 \cdot 10^{-3} = 6.2 \cdot 10^{-4}$ M.

4. Calculation of the concentration of the complex sulfates. The determination given above gives the total concentration of the rare-earth element in the solution, i.e., the sum of the concentrations of $Me^{\cdot\cdot\cdot}$ and $MeSO_4^{\cdot}$. For our calculations only the concentration of the $MeSO_4^{\cdot}$ ion is required. However, with a sufficiently large concentration of sulfuric acid when the excess of the sulfate ions is many times as great as the total concentration of the

rare-earth element, it is possible to consider that practically the entire concentration of the rare-earth element is found in the form of $MeSO_4^+$.

TABLE 4

Determined Dissociation Constants of Complex Sulfate

Exp. No.	Element	Concentration of sulfuric acid	pH	Total concentration		$[H_2C_2O_4]$ (M)	μ	f_1	f_2	Dissociation constant
				oxalic acid	rare-earth element					
1	lanthanum	0.1	1.08	$2.7 \cdot 10^{-3}$	$1.8 \cdot 10^{-3}$	$1.3 \cdot 10^{-3}$	0.2	0.7	0.40	$5.5 \cdot 10^{-4}$
2		0.1	1.08	$2.6 \cdot 10^{-3}$	$1.7 \cdot 10^{-3}$	$1.5 \cdot 10^{-3}$	0.2	0.7	0.40	$4.7 \cdot 10^{-4}$
3		0.05	1.35	$1.5 \cdot 10^{-3}$	$9.8 \cdot 10^{-4}$	$5.2 \cdot 10^{-4}$	0.1	0.8	0.46	$2.3 \cdot 10^{-4}$
4		0.05	1.35	$1.4 \cdot 10^{-3}$	$9.2 \cdot 10^{-4}$	$5.5 \cdot 10^{-4}$	0.1	0.8	0.46	$2.9 \cdot 10^{-4}$
5	cerium	0.1	0.96	$1.9 \cdot 10^{-3}$	$1.3 \cdot 10^{-3}$	$1.2 \cdot 10^{-3}$	0.2	0.7	0.40	$2.1 \cdot 10^{-3}$
6		0.1	0.96	$2.4 \cdot 10^{-3}$	$1.6 \cdot 10^{-3}$	$1.6 \cdot 10^{-3}$	0.2	0.7	0.40	$1.1 \cdot 10^{-3}$
7		0.05	1.28	$9.8 \cdot 10^{-4}$	$6.5 \cdot 10^{-4}$	$4.7 \cdot 10^{-4}$	0.1	0.8	0.46	$9.1 \cdot 10^{-4}$
8		0.05	1.28	$1.0 \cdot 10^{-3}$	$6.8 \cdot 10^{-4}$	$4.8 \cdot 10^{-4}$	0.1	0.8	0.46	$8.1 \cdot 10^{-4}$
9	praseodymium	0.1	1.04	$1.3 \cdot 10^{-3}$	$9.0 \cdot 10^{-4}$	$7.9 \cdot 10^{-4}$	0.2	0.7	0.40	$3.4 \cdot 10^{-3}$
10		0.1	1.04	$1.2 \cdot 10^{-3}$	$8.0 \cdot 10^{-4}$	$7.1 \cdot 10^{-4}$	0.2	0.7	0.40	$4.6 \cdot 10^{-3}$
11	neodymium	0.1	0.99	$2.2 \cdot 10^{-3}$	$1.5 \cdot 10^{-3}$	$1.4 \cdot 10^{-3}$	0.2	0.7	0.40	$1.2 \cdot 10^{-3}$
12		0.1	0.99	$1.8 \cdot 10^{-3}$	$1.3 \cdot 10^{-3}$	$1.1 \cdot 10^{-3}$	0.2	0.7	0.40	$2.0 \cdot 10^{-3}$
13		0.05	1.24	$1.08 \cdot 10^{-3}$	$7.2 \cdot 10^{-4}$	$5.4 \cdot 10^{-4}$	0.1	0.8	0.46	$8.9 \cdot 10^{-4}$
14		0.05	1.24	$1.1 \cdot 10^{-3}$	$7.4 \cdot 10^{-4}$	$5.5 \cdot 10^{-4}$	0.1	0.8	0.46	$8.5 \cdot 10^{-4}$

In carrying out the calculations, we used the values we had previously obtained for the solubility products of the oxalate of lanthanum, cerium and praseodymium. The solubility product of neodymium oxalate was taken as being equal to the corresponding value for praseodymium. The average results of several determinations are given in Table 4. The odd numbered experiments were carried out by means of volumetric determination of the total concentration, while the even numbered ones were done by gravimetric means.

The following are the average values for the dissociation constants that have been determined: $LaSO_4^+ = 3.8 \cdot 10^{-4}$, $CeSO_4^+ = 1.2 \cdot 10^{-3}$, $PrSO_4^+ = 4.0 \cdot 10^{-3}$, $NdSO_4^+ = 1.2 \cdot 10^{-3}$.

SUMMARY

1. It has been shown that the determination of the solubility products of slightly soluble oxalates by their solubility in hydrochloric acids gives fully satisfactory results.

2. It has been verified that the solubility products of lanthanum, cerium, and praseodymium are of the order of 10^{-28}.

3. The dissociation constants of the complex sulfates of lanthanum, cerium, praseodymium, and neodymium have been determined; they are of the order of 10^{-3}-10^{-4}.

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STUDY OF THE INTERACTION OF MOLYBDENUM COMPOUNDS WITH SODIUM CHLORIDE

I. INTERACTION OF MoO_3 WITH SODIUM CHLORIDE

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The interaction of molybdenum trioxide with sodium chloride can lead to the formation of sodium molybdate and molybdenum oxychlorides; the exact product depends on the reaction conditions (temperature, the availability of oxygen, and impurities). It is known that in the action of chlorine on MoO_3, the main product is the dioxydichloride MoO_2Cl_2, which is a yellow-white substance, easily sublimable at low temperatures. In accordance with this, the interaction of MoO_3 with sodium chloride in the presence of oxygen can be represented by the reaction:

$$MoO_3 + 2NaCl + 1/2O_2 = Na_2MoO_4 + Cl_2, \quad (1)$$

$$MoO_3 + Cl_2 = MoO_2Cl_2 + 1/2O_2. \quad (2)$$

In the absence of oxygen, the mechanism of the reaction may be described in another way: first the formation of the oxychloride and sodium oxide takes place, the latter then enters into a reaction with MoO_3. In this case the evolution of chlorine in general should not take place.

$$MoO_3 + 2NaCl = MoO_2Cl_2 + Na_2O, \quad (3)$$

$$MoO_3 + Na_2O = Na_2MoO_4, \quad (4)$$

$$2MoO_3 + 2NaCl = Na_2MoO_4 + MoO_2Cl_2. \quad (5)$$

In accordance with these ideas, the study of the reaction of the interaction of molybdenum trioxide with sodium chloride was carried out both in the air and in an inert gas atmosphere.

The Method of Investigation. A quartz boat containing the investigated substance (weight 3 g) was placed in a quartz tube which was heated by a tubular furnace. Air or an inert gas was drawn through the tube at a fixed rate (about 10 liters/hour). In each experiment we determined the quantity of chlorine evolved, the quantity of molybdenum sublimated, and the quantity of molybdenum leached out of the reaction products which remained in the combustion boat. For the collection of the chlorine, the gases were passed through a system of absorbers containing a potassium iodide solution. The molybdenum oxychloride was sublimated, being condensed in the cold part of the tube, and was carried into solution by means of successive treatment in tubes containing distilled water, dilute hydrochloric acid, and ammonia. The reaction products which remained in the boat were treated with distilled water with agitation for one hour at 85-90°.

The determination of molybdenum in the solutions and in the solid residues was carried out by gravimetric (plumbate) means.

The experiments were carried out at 400, 500, 600 and 700° for one hour.

Chemically pure compounds were used as raw materials; from these, mixtures of the components were prepared which had stoichiometric compositions corresponding to equation (1).

Interaction of Molybdenum Trioxide with Sodium Chloride in an Air Atmosphere.*

The results of this series of experiments are given in Table 1 and on Figures 1 and 2.

The data show that at 400° the speed of the reaction is negligible. Above 400° the speed of the reaction rises sharply: the evolution of chlorine is observed, the cold part of the tube is quickly filled with a goldish crystalline sublimate which becomes yellowish-white upon cooling. Investigation showed that the sublimate was molybdenum dioxydichloride MoO_2Cl_2 (Table 3).

* With the precipitation of V. Chernyæva.

It is evident from the data of Table 1 and Figures 1 and 2 that the interaction of molybdenum trioxide with sodium chloride in an air atmosphere takes place with the formation of sodium molybdate and molybdenum oxychloride, and with the evolution of free chlorine. With this, the formation of $NaMoO_4$ and MoO_2Cl_2 can occur both in accordance with reactions (1) and (2) and in accordance with reactions (3) and (4).

Analysis of the curves (Figs. 1 and 2) makes it possible to reach the conclusion that up to 500° the interaction of molybdenum trioxide and sodium chloride leads chiefly to the formation of sodium molybdate (80% of the total quantity of molybdenum). The portion of molybdenum which is sublimated in the form of MoO_2Cl_2 is comparatively small (15% of the total quantity of molybdenum).

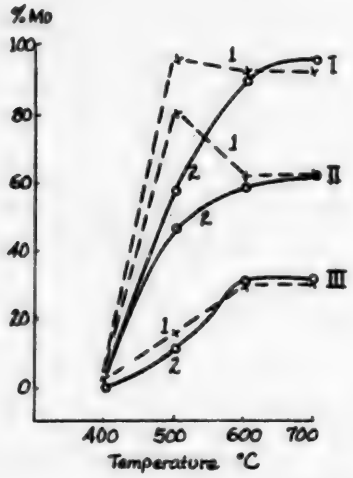

Fig. 1. Dependence of the extent of the formation of MoO_2Cl_2 and Na_2MoO_4 on the temperature for a mixture of MoO_3 and NaCl.
I) Total quantity of reacted molybdenum,
II) molybdenum leached out, III) molybdenum in the sublimates.
1) In an air atmosphere, 2) in an argon atmosphere.

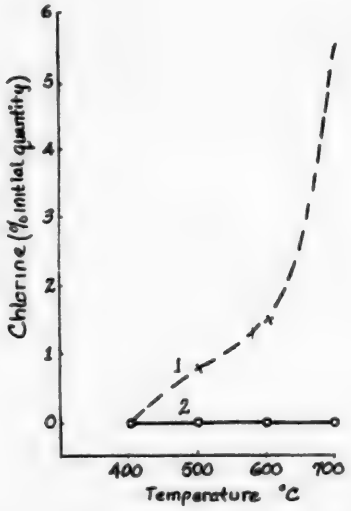

Fig. 2. Dependence of the quantity of chlorine given off on the temperature for mixtures of MoO_3 and NaCl. 1) In air atmosphere, 2) in argon atmosphere.

Since only an insignificant quantity of chlorine is given off at 500°, the formation of Na_2MoO_4 takes place chiefly according to equation (3).

At higher temperatures (600-700°), the quantity of molybdenum increases and the portion of molybdenum combined in the form of Na_2MoO_4 is correspondingly lowered. However, the quantity of chlorine which is given off at 600-700° is considerably larger than at 500°. Therefore, at these temperatures, the portion of MoO_3 reacting with NaCl in accordance with reaction (1) is increased.

It should be pointed out that the total quantity of reacted molybdenum trioxide reaches 93-97% when the reaction has been carried out for one hour in the temperature interval of 500-700°; this indicates the high speed with which the reaction takes place.

Interaction of MoO_3 with Sodium Chloride in an Inert Gas Atmosphere

The experiments were carried out in an atmosphere of argon which had been passed through a tube containing metallic calcium heated to 600° in order to purify it of admixtures of oxygen (0.05%). The results of the experiments are given in Table 2 and in Figs. 1 and 2.

In the absence of oxygen the evolution of chlorine was not observed at any of the investigated temperatures. At 500° and above, large quantities of the sublimates of the oxychloride are formed. The quantity of sublimated molybdenum increases with a rise in temperature and at 600-700° constitutes approximately 30% of the original molybdenum content. The quantity of molybdenum leached out also increases with a rise in temperature and at 600-700° constitutes approximately 60% of the original quantity of molybdenum.

TABLE 1

Interaction of MoO_3 and NaCl in an air atmosphere.
Original weight of charge 3.0 g including 1.12 g of molybdenum

Experiment No.	Temperature	Quantity of chlorine given off		Quantity of molybdenum sublimated		Leaching of the solid residue with water		Total reacted Mo (% of the initial quantity)
		(In g)	In % of the chlorine content in the original charge	(In g)	(In % of the initial quantity)	Mo in solution (in g)	(In % extracted from the original content)	
9	400°	None	None	0.0003	0.027	0.0239	2.13	2.16
10	400	None	None	0.00075	0.067	0.0251	2.24	2.30
11	500	0.00632	0.78	0.1706	15.23	0.8903	79.50	94.73
12	500	0.00747	0.92	0.1781	15.90	0.9289	82.94	98.84
13	600	0.0133	1.64	0.3223	28.77	0.7182	63.94	92.71
14	600	0.0115	1.42	0.3740	33.40	0.6756	60.30	93.70
15	700	0.0468	5.77	0.3523	31.45	0.6609	59.09	90.54
16	700	0.0449	5.54	0.3422	30.55	0.7171	64.02	94.57

TABLE 2

Interaction of MoO_3 with NaCl in an argon atmosphere.
Weight of charge 3.0 g including 1.12 g of molybdenum

Experiment No.	Temperature	Quantity of chlorine given off		Quantity of molybdenum sublimated		Leaching of the solid residue with water		Reacted Mo (in % of the original quantity)
		(In g)	(In % of the chlorine content in the charge)	(In g)	(In % of initial quantity	Molybdenum in solution (in g)	(In % extracted from the original content)	
30	400°	None	None	0.0015	0.13	0.0136	1.21	1.34
31	400	None	None	0.0010	0.09	0.0136	1.21	1.30
32	500	None	None	0.1223	10.92	0.532	47.50	58.42
33	500	None	None	0.1260	11.25	0.507	45.02	56.27
58	600	None	None	0.3427	30.60	0.6766	60.41	91.01
59	600	None	None	0.3530	31.51	0.6326	56.48	87.99
72	700	None	None	0.3305	29.5	–	–	–
73	700	None	None	0.3804	33.96	0.6844	62.00	95.96

TABLE 3

Chemical analysis of the oxychlorides

Temperature of the experiments	Oxychloride obtained in an atmosphere of			
	Air		Argon	
	% Mo	% Cl	% Mo	% Cl
500°	46.5	38.21	45.90	36.96
500	47.56	36.09	46.27	–
600	48.35	37.37	46.40	36.07
600	–	–	46.17	35.14
700	48.38	36.42	47.80	36.93
700	47.38	34.06	48.54	37.52
Average	47.23	36.43	46.85	36.52

The results of the experiments which we carried out confirm the hypothesis expressed above that in the absence of oxygen the interaction of molybdenum trioxide with sodium chloride takes place in accordance with equations (3) and (4); together with this, one would expect that the oxychloride and the sodium molybdate formed in accordance with equations (3) and (4) would each contain the same portions of the original quantity of molybdenum. However, the quantity of molybdenum linked in the form of Na_2MoO_4, is considerably larger than that combined in the form of MoO_2Cl_2. This is explained by the fact that sodium molybdate reacts with molybdenum trioxide, forming polymolybdates, e.g. $Na_2O \cdot 2MoO_3$, $Na_2O \cdot 4MoO_3$ (Fig. 3), which leads to an increase in the proportion of molybdenum which is leached out.

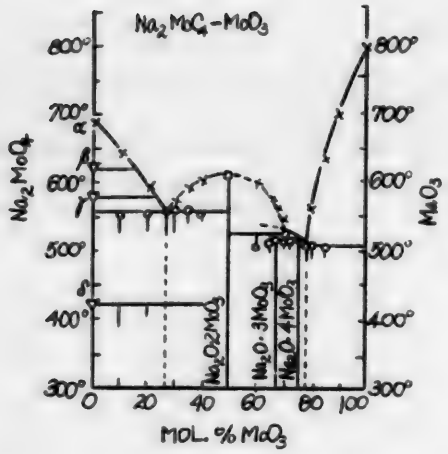

Fig. 3. The system $Na_2MoO_4-MoO_3$.

Analysis of the Oxychlorides

The sublimates of the oxychlorides, obtained as a result of the interaction of molybdenum trioxide and sodium chloride in an air atmosphere and in argon, were analyzed for their molybdenum and chlorine contents.

The results of the experiments are given in Table 3.

Comparison of the obtained data with the composition of the various oxychlorides of molybdenum shows that the sublimates are the oxychloride corresponding to the formula MoO_2Cl_2 (the theoretical contents of molybdenum and chlorine in molybdenum dioxydichloride are 48.24 and 35.67% respectively). The reaction between molybdenum trioxide and sodium chloride can serve as a convenient method for the preparation of the oxychloride.

SUMMARY

1. The reaction of molybdenum trioxide with sodium chloride in an air atmosphere and in an inert gas atmosphere has been studied.

2. In the investigated temperature range (400-700°) the reaction takes place with the formation of sodium molybdate and molybdenum dioxydichloride; the equilibrium is shifted in the direction of the formation of sodium molybdate in this temperature range.

3. In the presence of oxygen the interaction of MoO_3 and NaCl takes place according to equations (1-4) and is accompanied by the evolution of chlorine. In the absence of oxygen the reaction takes place in accordance with equations (3) and (4).

4. At temperatures above 500°, with stoichiometric porportions of the components, 94-96% of the molybdenum trioxide has reacted at the end of one hour.

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Non-Ferrous Metals and Gold

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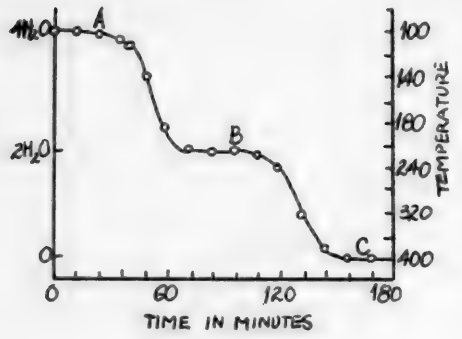

Hydrates of strontium metamobates.
A) $Sr(NbO_3)_2 \cdot 4H_2O$, B) $Sr(NbO_3)_2 \cdot 2H_2O$, C) $Sr(NbO_3)_2$.

The solution of strontium hydroxide was prepared separately for each test with the observation of the necessary precautions, since it absorbs carbon dioxide from the air very quickly. The strontium metaniobate precipitate was filtered, carefully washed, and dried at 100°.

The obtained salt was analyzed. Weight of sample 0.1339 g.

Found %: Nb_2O_5 61.1; SrO 23.59; H_2O 16.31. $Sr(NbO_3)_2 \cdot 4H_2O$. Calculated %: Nb_2O_5 60.18; SrO 23.53; H_2O 16.29.

It follows from the analysis that the substance prepared by us was strontium metaniobate, containing four molecules of water of crystallization.

2. Dehydration of $Sr(NbO_3)_2 \cdot 4H_2O$. In order to determine the composition and number of intermediate crystal hydrates of strontium metaniobate, we studied its dehydration with a continuous rise in temperature. This method, as was shown by Guichard [8], makes possible the establishment of the nature of the chemical bond between the molecules of water and the solid substance, i.e., it enables us to determine whether it is a hydrated bond or is maintained as a result of the action of special forces (adsorption forces) on the surface of the solid body. In the first case the system will be monovariant, in the second—divariant. Experiments on the dehydration of hydrates with rising temperatures require the simultaneous measurement of the weight of the substance and the temperature for each moment of time. This is accomplished through the use of spring microbalances of the type used by McBain and Bakr [9]. The loss of weight of the crystal hydrate sample, caused by its dissociation with a rise in temperature, is recorded by a microcathetometer. The temperature was measured with a mercury thermometer over a range of 500° with an accuracy of up to $\pm$ 2°.

The curve showing the dependence of the change of weight of $Sr(NbO_3)_2 \cdot 4H_2O$, with a continuously rising temperature, on time is given in the figure.

From the analysis of this curve it follows that the first horizontal section A, corresponds to the tetrahydate, which, judging by the slope of the curve, begins to dissociate to a considerable degree at 110° with the formation of a hydrate containing a smaller quantity of water of crystallization. The second horizontal section, B, corresponds in its composition to the dihydrate of strontium metaniobate. This compound, under the conditions of the experiment, was stable within the temperature range from 210 to 260°. Above 260° the dihydrate begins to dissociate, and at 390° it has almost completely decomposed with the formation of anhydrous strontium metaniobate (section C).

3. The solubility of $Sr(NbO_3)_2 \cdot 4H_2O$ was determined by radiometric means. A radioactive compound $Sr(NbO_3)_2 \cdot 4H_2O$, was prepared; it contained, along with ordinary strontium, the radioactive isotope of strontium Sr^{89}. The original preparation according to its β-radiation had an activity of 1054 pulses per minute for 1 mg of $Sr(NbO_3)_2 \cdot 4H_2O$. The measurements were made with a cylindrical β-counter on a calculating apparatus of the "B" type.

In order to determine the solubility, a weighed portion of about 0.5 g $Sr(NbO_3)_2 \cdot 4H_2O$ was introduced into a vessel (equipped with a stirrer) containing 200 ml of twice-distilled water. This vessel and its contents were kept for not less than 24 hours, with constant stirring, in an ultrathermostat in which the temperature was maintained at a constant level within $\pm$ 0.2°. The equilibrium was considered achieved when two samples of 15 ml each of a solution, filtered through an ultrafilter, taken eight hours apart, showed corresponding results on the β-counter (about 75 $\pm$ 4 pulses per minute). Simultaneously, the activity of a standard solution, prepared by the dissolution of 0.1554 g $Sr(NbO_3)_2 \cdot 4H_2O$ in 200 ml of concentrated nitric acid containing a small quantity of hydrogen peroxide was measured.

The determination of the solubility of $Sr(NbO_3)_2 \cdot 4H_2O$ was carried out at 15, 25 and 50°. The results are given in Table 1.

4. X-Ray Examination.* Structure of the Tetrahydrate of Strontium Metaniobate.

* With the participation of A. K. Shtolts.

TABLE 1

Solubility of $Sr(NbO_3)_2 \cdot 4H_2O$ in water

Temperature	Solubility	
	(In g/l)	(In M)
15°	0.00607	$1.4 \cdot 10^{-5}$
25	0.01032	$2.33 \cdot 10^{-4}$
50	0.01205	$2.72 \cdot 10^{-4}$

The compound was studied by the powder method. An X-ray photograph was produced using copper radiation in a camera with the radius of the cylindrical adapter R = 28.73 mm. The position of the lines on the X-ray photograph were determined with an accuracy of up to 0.2 mm. The intensity of the lines was evaluated visually.

The results of the determination of the interplanar distances in $Sr(NbO_3)_2 \cdot 4H_2O$ crystals and the intensity of the corresponding lines on the X-ray photograph are given in Table 2.

TABLE 2

Magnitude of the interplanar distances of the crystals $Sr(NbO_3)_2 \cdot 4H_2O$

Line Number	Intensity (I)	Distance (d)	Line Number	Intensity (I)	Distance (d)
1	Strong	3.50	12	Weak	1.443
2	Average	3.03	13	Average	1.415
3	Average	2.83	14	Weak	1.286
4	Strong	2.45	15	Weak	1.185
5	Average	2.27	16	Average	1.157
6	Average	2.13	17	Weak	1.073
7	Strong	2.03	18	Weak	1.057
8	Strong	1.91	19	Weak	0.966
9	Weak	1.81	20	Weak	0.896
10	Weak	1.73	21	Weak	0.882
11	Weak	1.55			

The hypothesis was expressed that the structure of this compound is similar to that of strontium nitrate in which the nitrogen atoms have been replaced by niobium atoms. The strontium atoms form a face-centered cubic lattice. The niobium ions are located in this lattice, but not in the centers of the eight octants; they are, rather, considerably askew. The $[NbO_3]^{1-}$ ions have the form of a triangle. The elementary cell, formed by the strontium ions, thus contains 4 strontium ions, 8 niobium ions, and 24 oxygen ions. In addition, 16 molecules of water enter into the composition of the cell.

The parameter of the lattice, a, calculated according to all the lines of the crystallogram, is equal to 8.56A.

Assuming the structure indicated above for the compound, and using the parameter of the lattice calculated from the crystallogram, it is possible to determine the density of the compound according to the formula

$$\delta = \frac{nA_{av.} \cdot 1.65 \cdot 10^{-24}}{Q},$$

where n is the number of ions in the elementary cell, $A_{av.}$ – the average atomic weight, and Q – the volume of the elementary cell.

The density of $Sr(NbO_3)_2 \cdot 4H_2O$, calculated in this way, is equal to 4.64 g/cm^3.

The density of this compound, determined with a pyknometer, is 4.663 g/cm^3 ; this confirms our hypothesis on the structure of $Sr(NbO_3)_2 \cdot 4H_2O$.

5. The melting point of anhydrous strontium metaniobate was determined from cooling and heating curves, using platinum-platinum and rhodium thermocouples. The thermocouples were calibrated from the melting points of the chemically pure salts KNO_3, KCl, Na_2SO_4 and K_2SO_4.

The melting point of anhydrous strontium metaniobate proved to be 1225 ± 20°.

SUMMARY

1. Strontium metaniobate and its tetrahydrate $Sr(NbO_3)_2 \cdot 4H_2O$ have been prepared.

2. The dihydrate of strontium metaniobate, $Sr(NbO_3)_2 \cdot 2H_2O$, has been detected by the method of dehydration with a continuous rise in temperature.

3. The solubility of $Sr(NbO_3)_2 \cdot 4H_2O$ at 15, 25 and 50° has been studied by radioactive means.

4. The parameter of the crystal lattice of $Sr(NbO_3)_2 \cdot 4H_2O$ has been determined; the value of the density of the compounds, obtained from this data, has been found to be in satisfactory agreement with that determined by pyknometric means.

5. The melting point of strontium metaniobate has been determined; it is 1225 ± 20°.

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THE ENTHALPY OF FORMATION OF LITHIUM STIBIDE

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Lithium stibide is formed on the direct interaction of the simple substances at high temperatures, or by the action of antimony on a solution of lithium in liquid ammonia.

We prepared lithium stibide by melting lithium and antimony, taken in stoichiometric proportions, in hermetically sealed steel crucibles. The melting was carried out over the course of several hours with frequent stirring and temperatures up to 1250°.

The X-ray photograph of the preparation obtained in this way showed the absence of free antimony; the interplanar distances found by us coincided with those obtained by Zintl [1]. It also turned out that on fusion no significant amount of iron, or other component of steel, was introduced in the preparation. The contents of lithium and antimony in the preparation were very close to those corresponding to the formula Li_3Sb. All the operations with lithium stibide were carried out in an atmosphere of dry carbon dioxide.

The enthalpy of formation was determined on the basis of the value for the enthalpy of solution of the stibide in dilute hydrochloric acid.

It had been established in preliminary experiments that about 1-2% of the antimony forms stibine under these conditions; since the enthalpy of formation of stibine is of a fairly large magnitude, this could introduce an important error in the determination of the heat of formation of Li_3Sb.

In order to exclude this possibility, we used in our calorimetric experiments, not a pure hydrochloric acid solution, but one which contained lithium stibide; the presence of finely-crushed antimony in the solution, as was shown by specially conducted experiments, reduces the quantity of stibine formed to practically zero.

The enthalpy of the reaction of the dissolution of Li_3Sb in hydrochloric acid was measured in an adiabatic calorimeter. An ampoule containing a weighed portion of the preparation was placed in a glass, hermetically sealed chamber into which was poured about 40 ml of hydrochloric acid (0.9 N). At the same time, the ampoule was broken with a glass spatula, which also served as a stirrer. The chamber was placed in a calorimetric vessel – a brass beaker with a capacity of about 2 liters, equipped with a stirrer. 1500 g of water was poured into this vessel.

The hydrogen which was formed in the process of solution was run through a glass coil, which guaranteed the possibility of heat exchange with the calorimeter.

The change in temperature of the calorimeter was established from the change in resistance (which was measured with a Wheatstone bridge with an accuracy up to 0.1Ω. Since a change in temperature of 1° corresponded to a change in resistance of 705Ω, this made possible the measurement of the temperature with an accurady of up to ~0.00015°.

The calorimetric vessel was placed in a brass jacket, which was in turn immersed in a vat of water, the temperature of which was kept constant at 25 ± 0.005°. The thermal capacity of the calorimeter was determined from the value of the enthalpy of solution of magnesium which had been prepared by vacuum distillation; it was 2.788 ± 0.017 cal /Ω. For the enthalpy of the process

$$Li_3Sb_{cr} + 3HCl_{s-s} = 3LiCl_{s-s} + 3/2H_2$$

(concentration of hydrochloric acid: 1 mole HCl to 80 moles H_2O) in three successive experiments, conducted with different preparations, the following values were obtained: −121.8, −123.0, −126.6 kcal/mole Li_3Sb. In conjunction with the enthalpies of formation of HCl and LiCl and the enthalpies of their solutions (corresponding to the concentrations of their solutions present in our calorimetric experiments) this gives for an enthalpy of formation of Li_3Sb −78.4, −77.2, and −73.7 kcal/mole.

The crystallogram of the preparation for which the enthalpy of formation was found to be equal to −73.7 kcal/mole, showed very weak lines for antimony. The first two values, on the other hand, were obtained for preparations for which the crystallograms showed no antimony lines. This gave us a basis for taking the average of the first two values, i.e., for proposing a value of −77.8 kcal/mole, for the enthalpy of formation of lithium stibide.

$$3Li_{cr} + Sb_{cr} = Li_3Sb + 77.8 \text{ kcal at } 25°.$$

A value of −55.0 kcal/mole was obtained for the enthalpy of formation of lithium bismuthide by Kubaschewski and Seitz [2]. Thus, in going from the antimonous compounds of lithium to the bismuthous compounds, a considerable lowering of the enthalpy of formation takes place. The same phenomenon is also observed for compounds of these elements with magnesium.

SUMMARY

The enthalpy of formation of lithium stibide at 25°, has been determined; it is equal to −77.8 kcal/mole.

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THE THERMAL STABILITY OF COPPER HALIDES

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Copper, on interaction with halides, gives two types of compounds, $CuHal_2$, and CuHal.

CuF_2, $CuCl_2$, $CuBr_2$,

CuF, CuCl, CuBr, CuI.

The compound which is the most stable thermally of the above copper halides is CuF_2. According to Watenberg [1], CuF_2 undergoes considerable dissociation only at temperatures above 600-700°C.

$$CuF_2 + 79.4 \text{ kcal} = CuF + \frac{1}{2} F_2.$$

$CuCl_2$ is decomposed at lower temperature (Proust [2]). Ephraim [3], Tarasenkov, Grigorovich and Boroslovskaya [4], heating $CuCl_2$ in a vacuum, determined its dissociation pressure directly. Jellinek and Koop [5] calculated the dissociation pressure of $CuCl_2$ on the basis of the equilibrium constants which they determined for the reduction of $CuCl_2$ by hydrogen at 251, 325 and 397°. The values calculated by Jellinek do not coincide with those obtained by direct methods by Ephraim and by Tarasenkov and co-workers (Fig. 1).

There is no data on the dissociation pressure of $CuBr_2$ in the literature. CuI_2 has not been obtained in solid form, although Fedotyev [6] observed Cu^{++} ions in aqueous solution on the action of an excess of iodine on suspended CuI.

Unlike CuF_2, CuF is thermodynamically unstable even at room temperature; the reaction of its disproportionnation is exothermic

$$2CuF - 29.4 \text{ kcal} = CuF_2 + Cu.$$

The fact that, on the reduction of CuF_2 with hydrogen, Jellinek and Rudat [7] always obtained metallic copper and not CuF, also indicates the instability of CuF. In contrast to copper fluoride, CuCl, CuBr and CuI are not inclined to disproportionation, and are decomposed thermally into the metal and the halogen only at very high temperatures. Copper chloride is the compound in this group which has been most throughly studied.

A great deal of work has been done on the reduction of copper chloride. One of the first workers in this field was Ribalkin [8], who reduced CuCl with hydrogen in sealed ampoules at 200-400°. Ribalkin did not determine the pressure in the ampoules and therefore his values are not comparable with those of other authors; but the great value of the work of Ribalkin consists in the fact that he was one of the few who studied the equilibrium of CuCl with hydrogen, both from the direction of the reaction of the reduction of CuCl with hydrogen, and from the direction of the oxidation of copper with hydrogen chloride. In addition, the equilibrium of the reduction of copper chloride was studied by Jellinek and Uloth [9], Parravano and Malquori [10], Watanabe [11], Kapustinsky [12], and Partington and Towndrow [13]. This reaction was studied over the widest temperature range by Watanabe. As is evident from Fig. 3, the data of Jellinek and that of Partington and Towndrow do not agree with that of the other authors.

The equilibria of the reduction of copper bromide and copper iodide with hydrogen were studied by Jellinek and his students Uloth [14] and Rudat [15]. The reduction of copper iodide with hydrogen was studied by them at 675-1100°C; at these temperatures, the dissociation of hydrogen iodide is of quite a large magnitude, but they did not take this circumstance into account in the calculation of the equilibrium constants; consequently, there is some doubt of the accuracy of their results.

In the present work, we have determined the dissociation pressure for copper (I) and copper (II) chloride, and for copper (I) and copper (II) bromide.

EXPERIMENTAL

Kahlbaumbrand "for analysis" quality $CuCl_2$ and $CuBr_2$ were used, being dehydrated before the experiments: $CuCl_2$ – by heating in a stream of hydrogen chloride (~ 150°), $CuBr_2$ – in a desiccator over phosphoric anhydride.

TABLE 1

Temperature °C	Temperature °K	P_{Cl_2} (in mm)	log P_{Cl_2} (in atm)	ΔF of the reaction (in calories)
219	492	0.5	−3.18	+6483
219	492	1.0	−2.88	+7158
219	492	0.5	−3.18	+6483
267	540	1.5	−2.705	+6683
305	578	3.5	−2.34	+6187
316	589	5.5	−2.14	+5766
320	593	6.0	−2.10	+5698
340	613	7.5	−2.01	+5638
343	616	8.5	−1.95	+5495
375	648	14.5	−1.72	+5099
392	665	19	−1.60	+4868
420	693	33	−1.36	+4311
440	713	37	−1.31	+4281
440	713	36.5	−1.32	+4301
458	731	61	−1.10	+3666
467	740	104.5	−0.86	+2924
495	768	200	−0.58	+2038

TABLE 2

Temperature °C	Temperature °K	P_{Br_2} (in mm)	log P_{Br_2} (in atm)	ΔF of the reaction (in calories)
130	403	2	−2.58	+4758
141	414	2.5	−2.48	+4702
150	423	4	−2.28	+4410
162	435	6	−2.10	+4184
170	443	8.5	−1.95	+3954
175	448	11	−1.84	+3772
180	453	14	−1.735	+3595
180	453	12	−1.80	+3735
182	455	13.5	−1.75	+3642
191	464	17	−1.65	+3610
199	472	24	−1.50	+3242
199	472	24	−1.50	+3242
210	483	36	−1.325	+2928
219	492	42	−1.26	+2832
219	492	41.5	−1.26	+2843
235	508	81	−0.97	+2265
235	508	84	−0.96	+2232
238	511	102	−0.87	+2034
248	521	126.5	−0.78	+1856
251	524	160	−0.68	+1622
270	543	250	−0.48	+1200
316	589	788	−0.02	− 42

Analysis of $CuCl_2$ gave, on the average, 47.23% Cu and 52.74% Cl. The theoretical values are 47.27% Cu and 52.73% Cl. Analysis of $CuBr_2$ gave on the average 28.36% Cu and 71.60% Br. The theoretical values are 28.45% Cu and 71.55% Br.

CuCl and CuBr were obtained by the gentle reduction of $CuCl_2$ and $CuBr_2$ with hydrogen. The temperature of the reduction did not rise above 200°. The proof that the reduction to the monovalent state was complete was the change in color of the salt to white, with the appearance of a small amount of copper.

Determination of the dissociation pressure of copper (II) chloride and copper (II) bromide. The dissociation pressure of copper (II) chloride and copper (II) bromide was determined directly by the statistical method of Johnston [3,4].

Copper (II) chloride begins to dissociate to a considerable extent above 200°; the bromide – above 150°. The value obtained for the dissociation pressure and for the free energy of the reaction $2CuHal_2 = 2CuHal + Hal_2$ are given in Tables 1 and 2. The vapor pressure of CuCl is extremely small at these temperatures and does not exceed the limits of error of the experiment. According to the data of Tarasenkov and Kozhmyakov [16], the vapor pressure of CuCl reaches 3.1 mm at 632°C, whereupon a $CuCl_2$ sublimate is not preserved in the cold part of the apparatus; it is therefore possible to consider that only chlorine is found in the gaseous phase.

From Table 1 it follows that

$$\log P^{*}_{Cl_2} = 3.061 - \frac{3113 \cdot 6}{T} \quad \text{from 219-436°C}$$

and

$$\log P_{Cl_2} = 8.508 - \frac{6979 \cdot 2}{T} \quad \text{above 436°C.}^{**}$$

From Table 2 it follows that

$$\log P_{Br_2} = 6.172 - \frac{3598 \cdot 3}{T} \quad \text{from 130-316°C.}$$

* The values for the dissociation pressure, entered under the logarithm sign, are expressed in atmospheres in all cases.

** Copper (I) chloride melts at 436°C.

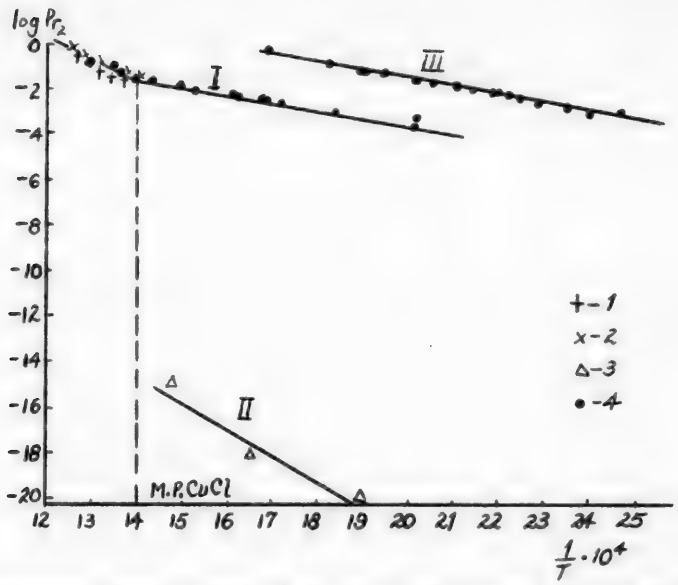

Fig. 1. Dependence of the logarithm of the dissociation pressure of copper (II) chloride and copper (II) bromide on 1/T.

I) $CuCl_2$, II) $CuCl_2$, III) $CuBr_2$.

1) Ephraim's data [3], 2) Tarasenkov's data [4], 3) Data of Jellinek and Koop [5], 4) Our data.

TABLE 3

Temperature		Composition of the equilibrium mixture (in %)		log K_e	$K_e = \frac{P^2_{HCl}}{P_{H_2}}$	Experimental error
°C	°K	H_2	HCl			
250	523	93.6	6.4	−2.337	0.0045	±0.0005
300	573	80.85	19.15	−1.315	0.048	±0.002
325	598	75.9	24.1	−1.071	0.085	±0.003
350	623	68.1	31.9	−0.796	0.16	±0.01

The vapor pressure of CuBr (Stell [17]) reaches 1 mm at 572°C.

The value for the dissociation pressure of $CuCl_2$ obtained by us, as is evident from Fig. 1, agrees with the data obtained by Ephraim and by Tarasenkov and co-workers as far as the order of magnitude is concerned. The values for the dissociation pressure calculated by Jellinek are of an entirely different order than those of the other authors (curve II, Fig. 1).

Determination of the dissociation pressure of copper (I) chloride and copper (I) bromide. Copper (I) chloride and copper (I) bromide are not decomposed to any significant extent even on heating to 800-900°C in a vacuum; it was therefore necessary to determine the dissociation pressures of these compounds indirectly by the determination of the equilibrium of some reaction in which the investigated substance takes part. We chose the reaction of the reduction of the halides with hydrogen. The method of the investigation was that of circulation. Equilibrium was approached from both directions (CuHal + H_2 and Cu + 2HHal). An excess of HHal was obtained by first heating the investigated substance in an atmosphere of hydrogen to 50-100° above the investigated temperature and then quickly cooling it to the temperature of the experiment. The pressure of the system was held constant during the experiment at 30-40 mm above atmospheric pressure. The partial pressures of the hydrogen and the hydrogen halide entering into the equation of the equilibrium constant of the reaction $K_e = P^2_{HHal}/P_{H_2}$, were calculated on the basis of the analysis of the gaseous reaction products. Further, by combining this equilibrium constant

with the equilibrium constant of the reaction of formation of the hydrogen halide, it is possible to calculate the dissociation pressure of the salt.

The reduction of copper (I) chloride with hydrogen was carried out at 250, 300, 325 and 350°C. The vapor pressure of copper (I) chloride at these temperatures, as has been pointed out above, is insignificant; it is therefore possible to consider that only hydrogen and hydrogen chloride were found in the gaseous state.

The average values for the equilibrium constants are given in Table 3.

From Table 3 it follows that

$$\log K_e = 5.789 - \frac{4102.6}{T}.$$

On the reduction of CuCl with hydrogen at temperatures lower than 325°C something like a false equilibrium is observed. The composition of the gaseous mixture obtained on the reduction of copper (I) chloride with hydrogen, which did not originally contain HCl, does not coincide with the composition of the gaseous mixture obtained on the oxidation of copper with hydrogen chloride, even though the ratio P^2_{HCl}/P_{H_2}, having reached a certain value, remained constant for a considerable length of time (from 10 to 20 hours). By gradually changing the original composition of the mixture of gases, we succeeded in obtaining values for P^2_{HCl}/P_{H_2} converging from both directions. Approximations of the equilibrium state for a number of experiments are shown on Fig. 2, where the change in the composition of the gaseous mixture is plotted against the time. It turned out that, in the case of the interaction of copper with hydrogen chloride (that is, in the case where the substance was first heated above the temperature of the experiment), the state of equilibrium was reached considerably more quickly than in the case when copper was reacted with hydrogen that either contained no HHal at all, or contained a very small amount of it.

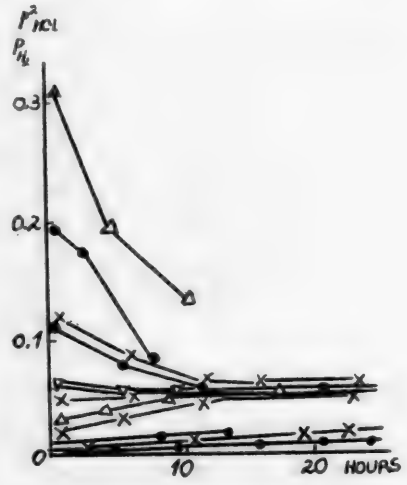

Fig. 2. Variation in composition of gaseous mixture upon approaching equilibrium at 300°C for the reaction $2CuCl + H_2 \rightleftharpoons 2Cu + 2HCl$.

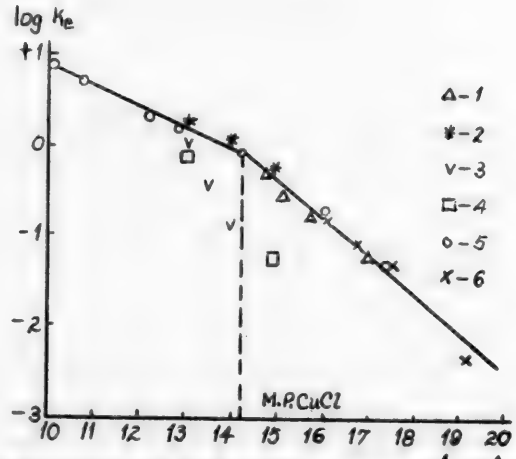

Fig. 3. Variation of log K_e of the reaction $2CuCl + H_2 \rightleftharpoons 2Cu + 2HCl$ with $1/T$.
1) Kapustinsky [12]; 2) Parravano and Maliquori [10]; 3) Jellinek [9]; 4) Partington and Townsdrow [13]; 5) Watanabe [11]; 6) our data.

The reduction of copper (I) bromide with hydrogen was carried out at 300, 315, 325, 340, 350, 375, 400, 480 and 550°C.

The average values obtained for the equilibrium constants of the reaction are given in Table 4.

From the data of Table 4, the log K_e can be determined.

$$\log K_e = 7.037 - \frac{5491.0}{T} \text{ from 300-350°C.}$$

TABLE 4

Temperature °C	Temperature °K	Composition of the gaseous equilibrium mixture (in %) H_2	Composition of the gaseous equilibrium mixture (in %) HBr	log K_e	$K_e = \frac{P^2_{HBr}}{P_{H_2}}$	Experimental error
300	573	94.1	5.9	−2.420	0.0038	±0.0002
315	588	92.55	7.45	−2.201	0.0063	±0.0007
325	598	90.6	9.4	−2.000	0.010	±0.001
340	613	89.0	11.0	−1.820	0.015	–
350	623	86.9	13.2	−1.658	0.022	±0.001
375	648	85.9	14.1	−1.620	0.024	–
400	673	83.1	16.9	−1.432	0.037	±0.002
480	753	79.0	21.0	−1.222	0.060	–
550	823	68.6	31.4	−0.796	0.16	±0.01

Just as in the case of copper (I) chloride, the reaction of the reduction of CuBr below 325°C without the preliminary heating of the salt takes place extremely slowly.

In Figs. 3 and 4, the dependence of the logarithms of the equilibrium constants on $1/T$ is plotted. While for copper (I) chloride, there is one inflection in the curve, corresponding to the melting point of CuCl, in the case of copper (I) bromide there are two such inflections: at a temperature above 350°, and at 480°C. Copper (I) bromide melts at 480°; therefore the inflection in the curve at the lower temperature corresponds to some change in the solid state. Monkemeyer [18] observed the transition α-CuBr ⇌ β-CuBr at 384°C, Krug and Sieg [19] determined the presence of three crystalline modifications of copper (I) bromide: γ-CuBr exists below 390°, β-exists from 391-470°, and α- exists from 470-488°; therefore, the inflection from 350-480° corresponds to a double change in the crystal lattice of copper (I) bromide.

As is evident from Figs. 1 and 3, the data obtained by Jellinek for $CuCl_2$ and CuCl is considerably different (often by several orders) from the data of the other authors. The same is true in the case of CuBr. The values obtained by us are considerably higher than those obtained by Jellinek at the same temperature (Fig. 4). The same is also true for a number of other compounds ($CrCl_3$, and $CrCl_2$ etc); in all these cases the values obtained by Jellinek were lower than those of the other authors. This circumstance can only be explained by defects in Jellinek's basic method. The essence of the method used by him for the study of heterogeneous equilibria (for example, of reduction) can be recalled briefly. A gas – the reducer – was passed at a specific rate of speed over the substance, which was in a furnace kept at a constant temperature. The compositions of the mixture of gases were determined for 2-3 different rates, and the values obtained were plotted on a graph: the rate of the reducing gas against the composition of the gaseous mixture; the curve so obtained was extrapolated to a value of zero for the rate of the gas. This extrapolated composition of the gaseous mixture was taken as the equilibrium composition.

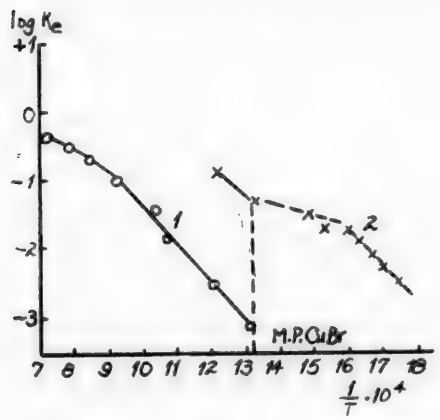

Fig. 4. Variation of log K_e of the reaction $2CuBr + H_2 \rightleftarrows 2Cu + 2HBr$ with $1/T$.
1) Jellinek's data [14]; 2) our data.

In addition to the difficulty of extrapolation from the observation of scattered points [20], there are also difficulties of a basic character*: at low temperatures the rate of flow of the gas, no matter how slow it may be, may be incomparably larger than the speed of the establishment of the equilibrium. In this case, the gases coming out of the furnace will be very far from the equilibrium composition, and the extrapolation can give low

* Jellinek himself determined the compositions of the mixture of gases at not more than three gas rates.

values. At higher temperatures, on the other hand, the speed of the establishment of the equilibrium can be incomparably greater than the speed of the flow of the gas, when even the first portions of the gas reduce the salt from the surface almost completely, and further portions will only dilute the gaseous mixture and thereby lessen the values obtained.• Therefore, in both cases, we will obtain values considerably lower than the true ones. Only in some rare cases, when the rate of flow of the gas, and the speed of the establishment of equilibrium are more or less commensurate, do the figures obtained by Jellinek agree with those of other authors; examples are the cases of $CoCl_2$ and $NiCl_2$ [21, 22].

DISCUSSION OF THE RESULTS

From the values obtained for the dissociation constants for the reaction of the reduction of CuHal with hydrogen and the equilibrium constants of the reaction of formation of the hydrogen halide, it is possible to obtain the values of the dissociation pressures of these compounds

$$2CuHal + H_2 = 2Cu + 2HHal,$$

$$K_e = \frac{P^2_{HHal}}{P_{H_2}} \text{ and } K_{HHal} = \frac{P^2_{HHal}}{P_{H_2} P_{Hal_2}},$$

$$P_{Hal_2} = \frac{P^2_{HHal}}{P_{H_2} K_{HHal}}, \quad P_{Hal_2} = \frac{K_e}{K_{HHal}}.$$

The values calculated in this way are given in Table 5.

From Table 5 it follows that

$$\log P_{Cl_2} = 5.012 - \frac{13809}{T} \text{ from 250-350°C,}$$

$$\log P_{Br_2} = 6.600 - \frac{11126}{T} \text{ from 300-350°C.}$$

The free energy, enthalpy, the entropy of formation of $CuCl_2$, CuCl, $CuBr_2$ and CuBr, calculated from the dissociation pressures, are given in Table 6. There is literature data for the thermal capacity of copper (I) and copper (II) chloride; therefore the values for ΔH and ΔS were given at 298°K for these compounds [23].

$$C_{P_{CuCl_2}} = 16 \cdot 80 + 0.0085 \cdot T,$$

$$C_{P_{CuCl}} = 10 \cdot 50 + 0.0097 \cdot T,$$

$$C_{P_{Cu}} = 5 \cdot 87 + 0.001 \cdot T - \frac{28700}{T^2},$$

$$C_{P_{Cl_2}} = 8 \cdot 77 + 0.00025 \cdot T.$$

On the formation of CuCl the entropy is lowered by 12.8 entropy units/mole, and on the formation of $CuCl_2$ by 32.9 entropy units/mole. The entropy of copper is equal to 7.97 entropy units/g-atom; the entropy of chlorine is equal to 53.31 entropy units/mole; hence the entropy of CuCl and $CuCl_2$ are equal, respectively, to 21.8 and 28.4 entropy units/mole.

In Fig. 5 is represented the dependence of the free energy of formation of the copper halides on the temperature. The free energy of formation of CuF_2, CuF and CuI were calculated from the data of Brewer's table [24]. The free energy of CuI_2 was calculated roughly by us from the formula $\Delta F = \Delta H - T\Delta S$, where ΔH is a value extrapolated by Britske and Kapustinsky [23] ($\Delta H = -4.8$ kcal/mole; taking into account the heat of sublimation of iodine, we obtain a value for ΔH on the order of -20 kcal/mole). For the entropy of copper (II) iodide, by analogy with the compounds of the other metals of the same decade of the periodic system with iodine, we took a value of 39 entropy units/mole. The value of ΔF in the case of CuI_2 was, of course, very approximate, but the order of the curve nevertheless remained the same. In the case of the fluorides, the free energy of CuF_2 was considerably more

• The work carried out by us to test Jellinek's method fully confirmed this hypothesis.

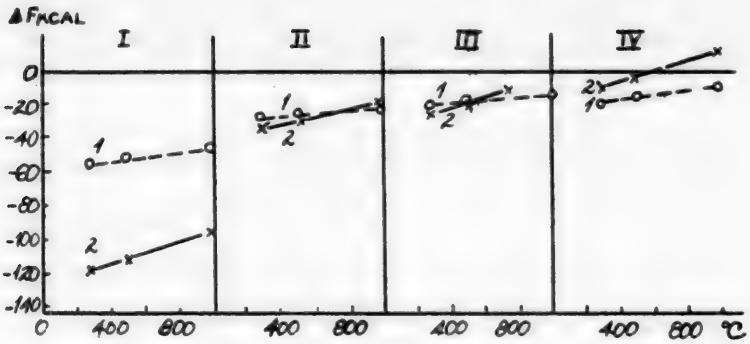

Fig. 5. Variation of the free energy of formation of copper halides with temperature. I) Fluorides: 1) CuF, 2) CuF_2; II) chlorides: 1) CuCl, 2) $CuCl_2$; III) bromides: 1) CuBr, 2) $CuBr_2$; IV) iodides: 1) CuI, 2) CuI_2.

TABLE 5

Temperature		CuCl			CuBr		
°C	°K	log K_e	log K_{HCl}	log P_{Cl_2}	log K_e	log K_{HBr}	log P_{Br_2}
250	523	−2.337	19.329	−21.666	–	–	–
300	573	−1.315	17.714	−19.029	−2.420	17.714	−12.816
315	588	–	–	–	−2.201	10.130	−12.331
325	598	−1.071	17.009	−18.080	−2.000	9.961	−11.961
340	613	–	–	–	−1.820	9.730	−11.550
350	623	−0.796	16.361	−17.157	−1.658	9.600	−11.258
375	648	–	–	–	−1.620	9.270	−10.890
400	673	–	–	–	−1.432	8.962	−10.392
401*	674	−0.286	15.185	−15.471	–	–	–
436	709	−0.061	14.482	−14.543	–	–	–
480	753	–	–	–	−1.222	8.113	− 9.335
507	780	+0.240	13.229	−12.989	–	–	–
550	823	–	–	–	−0.796	7.505	− 8.301
552	825	+0.340	12.546	−12.206	–	–	–
595	868	+0.535	11.963	−11.428	–	–	–
665	938	+0.736	11.131	−10.395	–	–	–
726	999	+0.878	10.487	− 9.609	–	–	–

TABLE 6

Substance	Temperature interval °K	ΔH kcal/mole	ΔS, entropy unit/mole**	ΔF_{298} cal/mole	ΔH_{298} kcal/mole	ΔS_{298} entropy unit/mole
CuCl	523-623	–	–	−27732	−31.9	−12.8
$CuCl_2$	492-768	–	–	−31400	−41.2	−32.9
CuBr***	573-623	−25.4	−15.1	−21952	–	–
$CuBr_2$	403-589	−32.0	−26.3	−24210	–	–

* Data for CuCl at 401° was taken from Watanabe [11].

** Entropy unit.

*** In the case of the bromides, all thermodynamic values were calculated for the formation of the bromide from gaseous bromine.

negative than the free energy of CuF; this leads us to the conclusion that CuF must undergo disproportionation, since the expenditure of energy on its decomposition is more than compensated for by the gain of energy on the formation of CuF_2. The slopes of the curves are not the same; therefore, one may expect that the exothermic character of the process of disproportionation gradually falls, and that at high temperatures the possibility of the existence of CuF becomes more probable.

With a transition from the fluorides to the iodides of copper (I), we see that the free energy curves rise higher and higher; in addition, the curve of $CuHal_2$ rises more quickly and at a sharper angle than the CuHal curve. This leads to the crossing of the curves (in the case of $CuCl_x$ and $CuBr_x$); the crossing of the $CuBr_x$ curves takes place at lower temperatures than in the case of $CuCl_x$. In the case of CuI_x, however, the exchange of places of the curves takes place. The curves of free energy of CuI_2 lies above that of CuI at all temperatures. Such a position of the curves leads to the thermal dissociation of $CuCl_2$ and $CuBr_2$ at comparatively low temperatures, and to the disappearance of CuI_2, since it is exothermically decomposed into CuI and iodine.

SUMMARY

1. The dissociation pressure of $CuCl_2$ was investigated by a statistical method in the temperature range from 219 to 495°C.

2. First, the dissociation pressure of $CuBr_2$ was investigated statistically in the temperature range from 130 to 316°C.

3. The equilibrium which was established on the reduction of CuCl with hydrogen in the temperature range from 250 to 350°C has been investigated.

4. The equilibrium which was established on the reduction of CuBr with hydrogen in the interval from 300 to 550°C has been investigated.

5. It has been shown that on the curve $\log K_e \Delta/T$ in the case of CuBr there are two inflections – one corresponding to the melting point of CuBr at 480°C, and the other at ~350°C, corresponding to the transition from one crystalline modification to another.

6. The enthalpy and the entropy of formation of $CuCl_2$, $CuBr_2$, CuCl and CuBr have been calculated.

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INVESTIGATION OF THE TERNARY SYSTEMS OF THE CHLORIDES, SULFATES AND TUNGSTATES OF LITHIUM AND POTASSIUM. I

A. G. Bergman, A. I. Kislova and V. I. Posypaiko

The investigation of the ternary systems Li||Cl, SO_4, WO_4 and K||Cl, SO_4, WO_4 is one of a series of studies which we are carrying out on the tungstates of the alkali metals lithium and potassium. The purpose of these investigations is the clarification of the interrelationship between the double decomposition reaction and that of complex formation; this relationship determines the character of the diagrams of the systems. After studying these two factors in the ternary system Li, K||SO_4, WO_4, we established its character as a system of the adiagonal-zone type. [1] This system is one of the three outer faces of the quarternary system Li, K||Cl, SO_4, WO_4. The above-mentioned ternary systems Li||Cl, SO_4, WO_4 and K||Cl, SO_4, WO_4 are the upper and lower bases of a right triangular prism, in which form quarternary reciprocal systems are usually represented (Fig. 1) [2].

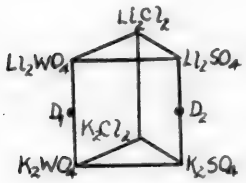

Fig. 1. Scheme of the prism Li, K||Cl, SO_4, WO_4.

EXPERIMENTAL

The systems were investigated by the visual-polythermal method, which has a number of advantages in investigations of systems with three and four components [3]; this method has been sufficiently described in the literature [4]. We will give briefly the characteristics of the components of the investigated ternary systems, Li,|| Cl, SO_4, WO_4 and K||Cl, SO_4, WO_4:

Component	Melting point	Transformations
Lithium chloride	606°	Homeomorphic - 565°
Lithium sulfate	860	Heteromorphic - 572°
Lithium tungstate	738	Heteromorphic - 660°
Potassium chloride	774	Homeomorphic - 27, 374
Potassium sulfate	1069	–
Potassium tungstate	1926	–

The Ternary System of the Chlorides, Sulfates, and Tungstates of Lithium

The ternary system Li||Cl, SO_4, WO_4 enters into the composition of the quarternary system Li, K||Cl, SO_4, WO_4 and was studied as the upper triangular base of the right triangular prism. The binary lateral sides of the ternary system Li||Cl, SO_4, WO_4 consist of:

1) The system Li_2Cl_2-Li_2WO_4 studied by Bergman and Kislova, has a eutectic at 490° and 41.5% Li_2WO_4; the polymorphic transformation of Li_2WO_4 was noted at 660° and 77.5% Li_2WO_4 and the homeomorphic transformation of Li_2Cl_2 was noted at 565° and 16.5% Li_2Cl_2.

2) the system Li_2WO_4-Li_2SO_4 was studied by the same authors; the eutectic was established at 68% Li_2SO_4 and 596°; the side of Li_2WO_4 was complicated at 660° and 37.5% Li_2SO_4 by polymorphic transformation;

3) the system Li_2Cl_2-Li_2SO_4 studied by Klochko [5] and repeated by Bergman and Akopov [6].

The eutectic system consisted of two basic branches; on the branch of Li_2Cl_2 homeomorphic transformation takes place at 81.5% Li_2Cl_2 and 565°. The eutectic corresponds to 46.5% Li_2Cl_2 and 478°; on the branch of Li_2SO_4, polymorphic transformation takes place at 572° and 87.5% Li_2SO_4.

The characteristic points of these systems are given in Table 1.

The fusion diagrams of the binary systems are given in Fig. 2 and Table 2.

TABLE 1

Characteristic points of the binary systems

No.	Binary Systems	Characteristic points of the system	Our data		Data of other authors	
			(%)*	Melting point	(%)*	Melting point
1	$Li_2Cl_2 - Li_2WO_4$	Eutectic	41.5 Li_2WO_4	490°	–	–
		Polymorphic transformation	77.5 Li_2WO_4	660	–	–
		Polymorphic transformation	16.5 Li_2Cl_2	565	–	–
2	$Li_2WO_4 - Li_2SO_4$	Eutectic	68 Li_2SO_4	596	–	–
		Polymorphic transformation	37.5 Li_2SO_4	660	–	–
3	$Li_2Cl_2 - Li_2SO_4$	Eutectic	–	–	46.5 Li_2Cl_2	478° [5]
		Homeomorphic transformation	–	–	81.5 Li_2Cl_2	565
		Polymorphic transformation	–	–	87.5 Li_2SO_4	572

* In equilmolecular percentages of the added component.

TABLE 2

Binary systems

$Li_2Cl_2 - Li_2WO_4$		$Li_2WO_4 - Li_2SO_4$				$Li_2Cl_2 - Li_2SO_4$			
Li_2WO_4 (in %)	Temperature	Li_2SO_4 (in %)	Temperature	Li_2SO_4 (in %)	Temperature	Li_2SO_4 (in %)	Temperature	Li_2SO_4 (in %)	Temperature
0	606	0	738	57.5	620	0	606	88	610
5	592	2.5	734	60	614	6.3	593	90	628
10	580	5	730	62.5	608	11.9	582	93	695
15	568	7.5	724	65	600	18.0	566	95.5	740
20	552	10	720	68	596	24.5	555	100	852
25	540	12.5	716	70	614	31.1	538		
27	534	15	712	72.5	634	38.2	526		
30	524	17.5	705	75	652	40.4	520		
32	518	20	702	77.5	674	42.5	515		
35	512	22.5	696	80	690	44.5	509		
37	502	25	690	82.5	710	46.6	501		
40	496	27.5	685	85	734	48.7	495		
45	510	30	680	87.5	756	50.6	490		
50	530	32.5	674	90	776	52.5	482		
55	550	35	666	92.5	800	54.5	482		
60	580	37.5	660	95	818	56.1	488		
65	602	40	656	97.5	842	57.9	494		
70	626	42.5	652	100	860	60.6	503		
75	650	45	648			65.7	519		
77	660	47.5	644			70.7	538		
80	670	50	636			76.5	552		
85	692	52.5	634			82	568		
100	738	55	624			86	590		

Internal Cuts

The results of the investigation of 7 internal sections are given in Table 3 and on Fig. 3.

A Brief Description of the Cuts

Cut 1. 65% Li_2Cl_2 + 35% Li_2WO_4 → Li_2SO_4 intersects: β-Li_2Cl_2, β-Li_2WO_4, β-Li_2SO_4, α-Li_2SO_4 respectively at 450° and 20% Li_2SO_4, 450° and 43% Li_2SO_4, 572° and 82.5% Li_2SO_4.

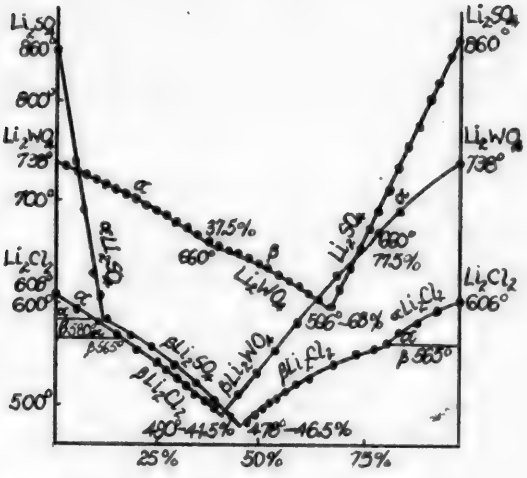

Fig. 2. The Binary Lateral Sides of the Ternary System Li ||Cl, SO_4, WO_4.

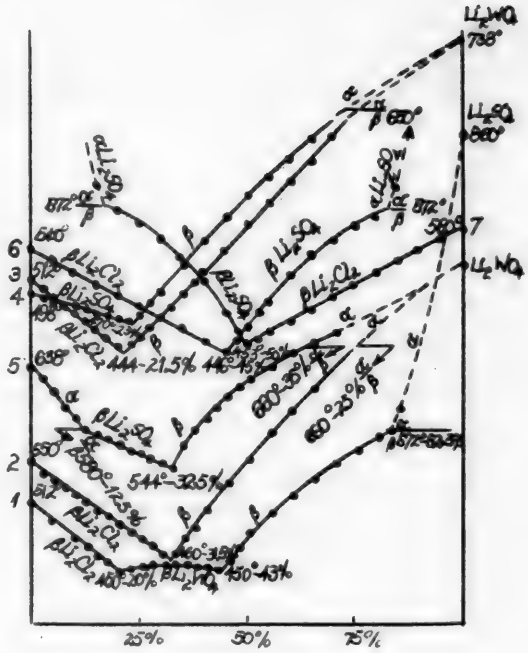

Fig. 3. Internal sections of the system Li || Cl, SO_4, WO_4.

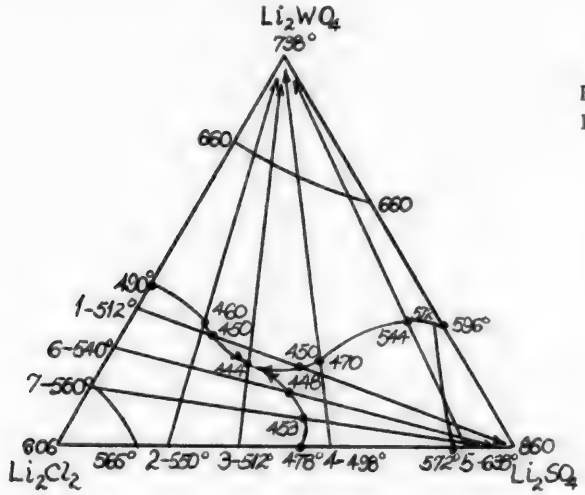

Fig. 4. Direction of the internal cuts.

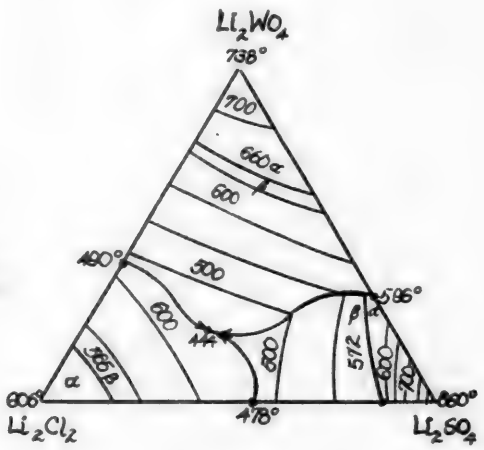

Fig. 5. Projection diagram of the system Li || Cl, SO_4, WO_4 on the triangle of composition.

Cut 2. 75% Li_2Cl_2 + 25% Li_2SO_4 → Li_2WO_4 intersects: β-Li_2Cl_2, β-Li_2WO_4, α-Li_2WO_4, respectively, at 460° and 31.5% Li_2WO_4, 660° and 75% Li_2WO_4.

Cut 3. 60% Li_2Cl_2 + 40% Li_2SO_4 → Li_2WO_4 intersects: β-Li_2Cl_2, β-Li_2WO_4, α-Li_2WO_4, respectively, at 444° and 21.5% Li_2WO_4, 660° and 73% Li_2WO_4.

Cut 4. 40% Li_2Cl_2 + 60% Li_2SO_4 → Li_2WO_4 passes through the field β-Li_2SO_4, β- and α-Li_2WO_4 at 470° and 23% Li_2WO_4, 660° and 70% Li_2WO_4.

Cut 5. 90% Li_2SO_4 + 10% Li_2Cl_2 → Li_2WO_4 intersects: α-Li_2SO_4, β-Li_2SO_4, β-Li_2WO_4, α-Li_2WO_4 at 580° and 12.5% Li_2WO_4, 544° and 32.5% Li_2WO_4, 660° and 35% Li_2WO_4.

TABLE 3

Internal cuts

Cut 1		Cut 2		Cut 3		Cut 4		Cut 5		Cut 6		Cut 7	
Li_2SO_4 (in %)	Temperature	Li_2WO_4 (in %)	Temperature	Li_2WO_4 (in %)	Temperature	Li_2WO_4 (in %)	Temperature	Li_2WO_4 (in %)	Temperature	Li_2SO_4 (in %)	Temperature	Li_2SO_4 (in %)	Temperature
0	512°	0	550°	0	512°	0	498°	0	638°	0	540°	0	560°
5	494	2.5	538	2.5	503	2,5	494	2.5	628	5	530	5	550
10	478	5	532	5	594	5	490	5	616	10	518	10	540
12.5	470	7.5	525	7.5	485	7.5	487	7.5	600	15	506	15	530
15	464	10	518	10	480	10	484	10	592	20	495	20	518
17.5	458	12,5	512	12.5	475	12,5	482	12.5	580	25	486	25	505
20	450	15	505	15	465	15	480	15	576	30	475	30	494
22.5	450	17.5	500	17.5	458	17.5	477	17.5	572	35	466	35	482
25	452	20	495	20	450	20	474	20	568	40	456	40	470
27.5	454	22.5	485	22.5	450	22.5	472	22.5	562	45	448	45	462
30	456	25	480	25	458	25	478	25	557	47.5	456	47.5	457
32.5	456	27.5	474	27.5	468	27.5	490	27.5	554	50	468	50	453
35	454	30	464	30	475	30	500	30	550	52.5	480	52.5	462
37.5	452	32.5	464	32.5	485	35	524	32.5	544	55	490	55	480
40	452	35	478	35	498	40	550	35	566	60	518	60	510
42.5	450	37.5	490	37.5	508	45	570	37.5	580	65	536	65	530
45	458	40	508	40	518	50	590	40	590	70	546	70	550
47.5	470	45	530	45	540	55	608	42.5	600	75	560	75	564
50	484	50	550	50	564	60	624	45	612	80	574	80	580
55	504	55	578	55	584	65	634	47.5	620	85	600	85	600
60	520	60	698	60	604	70	660	50	628	–	–	–	–
65	536	65	618	65	624	–	–	55	640	–	–	–	–
70	552	–	–	70	650	–	–	60	652	–	–	–	–
75	562	–	–	–	–	–	–	65	662	–	–	–	–
80	575	–	–	–	–	–	–	70	672	–	–	–	–
82.5	580	–	–	–	–	–	–	–	–	–	–	–	–
85	600	–	–	–	–	–	–	–	–	–	–	–	–

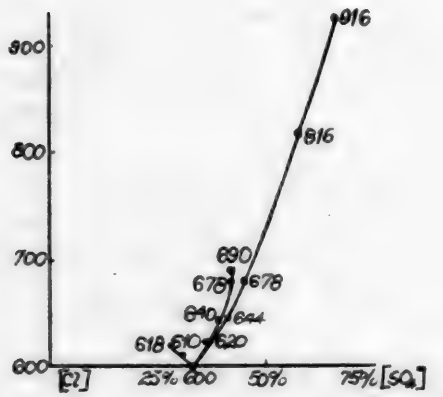

Fig. 6. Projection of the lines of common crystallization of the system Li ||Cl, SO_4, WO_4 on the side of Li_2Cl_2 – Li_2SO_4.

Cut. 6. 75% Li_2Cl_2 + 25% Li_2WO_4 → Li_2SO_4, intersects: β-Li_2Cl_2, β- and α-Li_2SO_4 at 446° and 45% Li_2SO_4, 530° at 83% Li_2SO_4.

Cut 7. 85% Li_2Cl_2 + 15% Li_2WO_4 → Li_2SO_4 passes through the fields β-Li_2Cl_2, β- and α-Li_2SO_4 at 453° and 50% Li_2SO_4, 572° at 85% Li_2SO_4.

Fig. 4 shows the scheme of the internal cuts.

Fig. 5 shows the projection diagram of the composition of the investigated ternary reciprocal system. Isotherms are given 50° apart; the polymorphic transformations of the components are shown correspondingly. In order to make the monovariant crystallization curves and the positions of the non-variant triple points in the system more exact, a projection of the common curves of crystallization of the triangle of composition on the Li_2Cl_2 – Li_2SO_4 side (Fig. 6), was constructed.

The diagram of the crystallization surface of the system consists of 3 fields of crystallization of the components, each field being further divided into the α- and β- sections.

The area, occupied by each field of crystallization, compared to the area of the triangle, is as follows (in %): LiCl – 26.44, α-modification, LiCl – 23.38, β-modification, LiCl – 3.06, Li_2WO_4 – 50.32, α-modification Li_2WO_4 – 8.81, β-modification, Li_2WO_4 – 41.51, Li_2SO_4 – 23.24, α-modification Li_2SO_4 – 4.94, β-modification Li_2SO_4 – 18.30.

SUMMARY

1. The ternary system Li‖Cl, SO_4, WO_4 has been investigated by the method of fusibility.

2. The system is simple, consists of 3 fields of crystallization with further division into the α- and β-modifications of the components. The largest area is occupied by the field Li_2WO_4 – 50.32%.

3. There is one triple eutectic point in the system at 444° of the composition 32% Li_2SO_4, 47% Li_2Cl_2, 21% Li_2WO_4.

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THE RECIPROCAL SYSTEM OF THE CHLORIDES AND SULFATES OF LITHIUM AND CALCIUM

M. S. Golubeva and A. G. Bergman

The considerable quantity of data which has been accumulated on chloride-sulfate exchange in melts makes apparent a certain periodicity, observed on the interaction of the chlorides and sulfates of various metals, depending on the position of the metals in the periodic system.

It is of particular interest to confirm experimentally the tendency, which has been noted previously, toward the weakening of complex-formation in reciprocal systems of the chloride-sulfate series of the mono- and divalent metals upon the systematic replacement of sodium and lithium by potassium in a system containing one and the same divalent metal [1-9].

The present investigation of the reciprocal system $Li,Ca \parallel Cl,SO_4$, along with the previously investigated systems $K,Ca \parallel Cl,SO_4$ [3] and $Na,Ca \parallel Cl,SO_4$ [4], makes this series complete.

At the same time, we have kept in mind the question of the confirmation of the correspondence between the conditionally calculated heat effect of the exchange reaction and the character of the diagram of the system [10].

EXPERIMENTAL•

The visual-polythermal method was utilized in the study of this system. The work was carried out in Pt crucibles in shaft electric furnaces. Thermocouples of alloys of Au,Pd,Pt-Pt,Rh were used. All compositions are expressed in equimolecular percentages. The melting points of the salts are: LiCl 609°, Li_2SO_4 852°, $CaCl_2$ 774°. The melting point of $CaSO_4$ has been taken conditionally from the literature [11] as being equal to 1450°.

Binary Systems

The previously studied systems: 1) Li_2Cl_2-Li_2SO_4 [12, 13], 2) Li_2Cl_2-$CaCl_2$ [14], 3) Li_2SO_4-$CaSO_4$ [15], 4) $CaCl_2$-$CaSO_4$ [16] were repeated by us. They are simple systems, with eutectics located, according to our data, at 480° and 52.5% Li_2SO_4 in the first of these systems, at 475° and 53% $CaCl_2$ in the second system, at 706° and 16.2% $CaSO_4$ in the third system, and at 708° and 12.5% $CaSO_4$ in the fourth system.

For the crystallization branches of $LiSO_4$ inflexions are observed in all cases at 572°; this corresponds to the heteromorphic transformation of this salt. On the branch of LiCl homeomorphic transformation occurs at 566°.

Diagonal sections. Studied previously [17] and repeated by us.
1. Li_2Cl_2-$CaSO_4$ is a stable diagonal section of the reciprocal system; the eutectic point, according to our data, is at 533° and 25% $CaSO_4$. 2. $CaCl_2$-Li_2SO_4 intersects the fields of the product of exchange of $CaSO_4$ respectively, according to our data, at 627° and 13.5% and 600° and 87.5% $LiSO_4$.

Internal cuts (Table 1 and Fig. 3). Eight internal cuts were studied; their distribution is shown on Fig. 2.

The crystallization surface of the reciprocal system (Fig. 4) is divided into the four crystallization fields of the components.

The largest single crystallization area (Table 2) occupies 76% of the total area; it is the field of the component with the highest melting point – $CaSO_4$.

Triangulation of the system into two-phase triangles is accomplished by means of the stable diagonal section Li_2Cl_2-$CaSO_4$.

With the projection of the curves of common crystallization on the sides of the composition area, a regular

• With the participation of T. T. Logacheva.

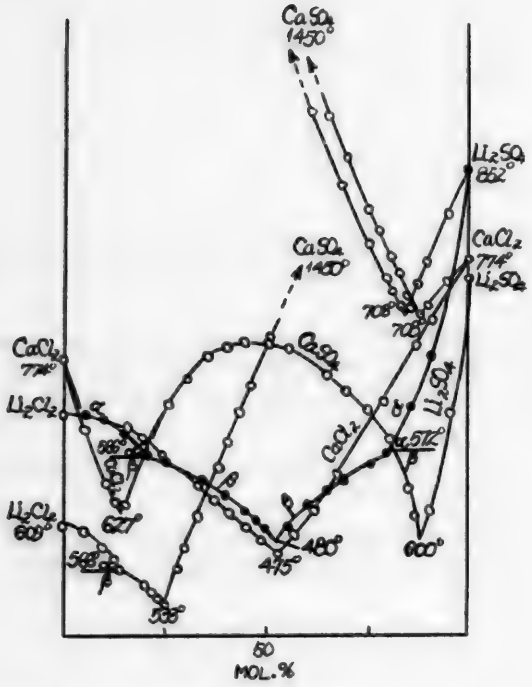

Fig. 1. Lateral sides and diagonal sections of the reciprocal system Li, Ca || Cl, SO_4.

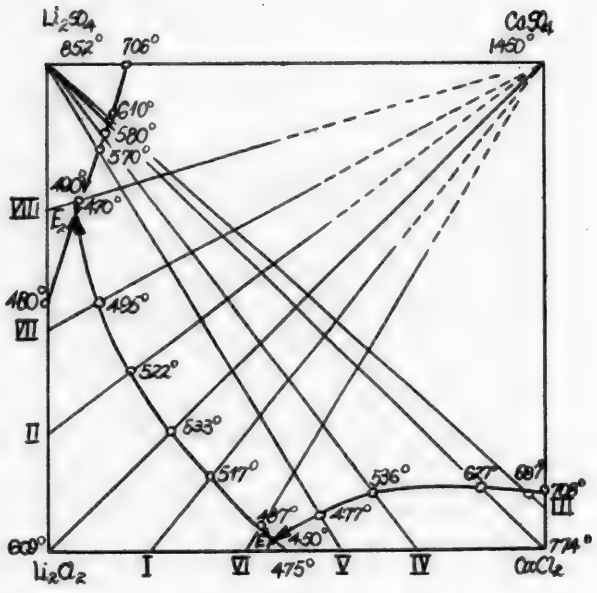

Fig. 2. Distribution of the internal cuts in the system Li, Ca || Cl, SO_4.

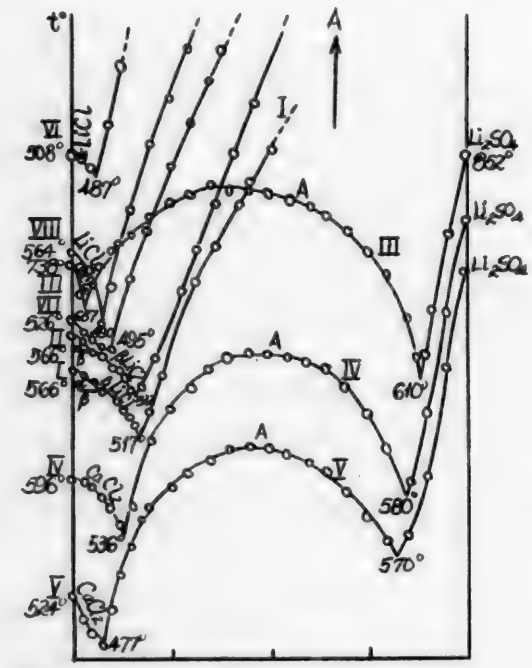

Fig. 3. Cuts through the reciprocal system Li, Ca || Cl, SO_4.
Direction of cuts I, II, VI, VII and VIII toward $CaSO_4$. A) $CaSO_4$.

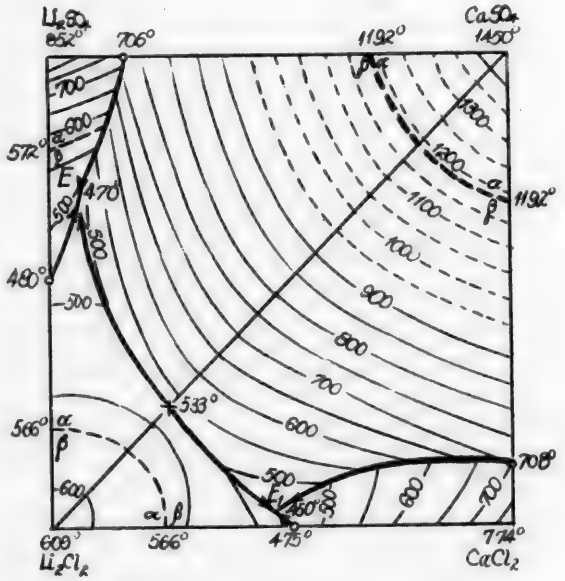

Fig. 4. Projection of the three dimensional diagram of the reciprocal system Li, Ca || Cl, SO_4 on the composition square.

TABLE 1

A – Original composition, B – added component; in the first column is given the molecular percentage of the added component, in the second column, the temperature of the appearance of the first crystals

1	2
Cut I	
A – 20% $CaCl_2$, 80% Li_2Cl_2	
B – $CaSO_4$	
0	584
2.5	580
5	570
7.5	560
11	554
13	542
14	534
16	526
19.5	540
22	580
31	673
36	711
42	752
45	744
50	808
P* 17	517
Cut II	
A – 25% $LiSO_4$, 75% Li_2Cl_2	
B – $CaSO_4$	
0	584
2.5	577
5	568
7.5	562
10.5	550
12	546
13.5	541
15	528
18	531
22	562
28	628
32	672
36.5	720
41	768
46.5	820
54	900
P* 16.5	522
Cut III	
A – 10% $CaSO_4$, 90% $CaCl_2$	
B – Li_2SO_4	
0	738
2.5	706
5	716
7.5	736
10	750
15	766
20	785
25	800
30	812
35	817
40	816
45	815
50	813
55	806
60	800
65	790
70	772
75	750
80	726
85	684
87.5	646
90	650
95	770
P_1 3.5	687
P_2 88.5	610
Cut IV	
A – 25% Li_2Cl_2, 75% $CaCl_2$	
B – Li_2SO_4	
0	596
2.5	591
5	587
7.5	574
10	562
12.5	547
15	566
20	634
25	666
30	688
35	708
40	716
45	720
50	722
55	719
60	714
65	706
70	688
75	658
80	624
85	586
90	660
95	760
P_1 13	536
P_2 85	580
Cut V	
A – 40% Li_2Cl_2, 60% $CaCl_2$	
B – Li_2SO_4	
0	524
2.5	500
5	486
7.5	474
10	507
12.5	542
15	574
17.5	600
20	614
25	634
30	648
35	660
40	670
45	673
50	672
60	657
65	648
70	632
75	603
80	582
85	586
90	648
95	756
P_1 7.5	477
P_2 82.5	570
Cut VI	
A – 40% $CaCl_2$, 60% Li_2Cl_2	
B – $CaSO_4$	
0	508
2.5	503
5	494
10	540
12.5	600
P 6.2	487
Cut VII	
A – 45% Li_2SO_4, 55% Li_2Cl_2	
B – $CaSO_4$	
0	526
2.5	514
5	507
7.5	500
10	495
15	565
20	617
25	680
30	726
35	768
40	817
50	910
P 10	495
Cut VIII	
A – 30% Li_2Cl_2, 70% Li_2SO_4	
B – $CaSO_4$	
0	564
5	546
7.5	490
10	530
12.5	570
15	608
20	675
25	722
30	772
35	826
40	870
45	924
P 7.5	490

* P – Points of intersection of the crystallization curves.

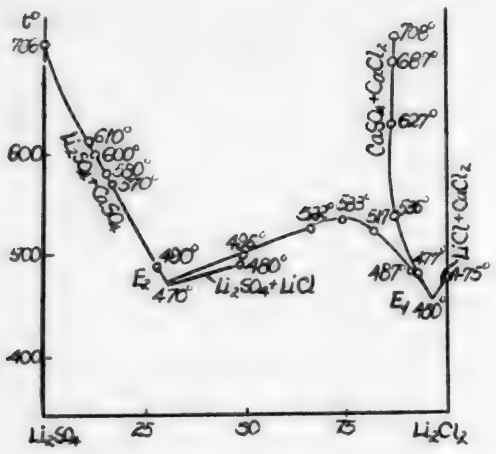

Fig. 5. Projection of the curves of common crystallization of the reciprocal system Li, Ca || Cl, SO_4 on the side of Li_2SO_4-Li_2Cl_2.

TABLE 2

Areas of the fields of crystallization

Name of the field of crystallization	Percentage of the total area occupied by the given field
$CaSO_4$	76
LiCl	14
Li_2SO_4	4.3
$CaCl_2$	5.7

fall in temperature and a full correspondence of the distribution of these curves and the multiple points is observed. One of these projections is shown in Fig. 5. The isotherms in the field of $CaSO_4$ form the clearly expressed ridge, deflecting somewhat in the direction of Li_2SO_4 from the plane of the stable diagonal; this shows a tendency toward an exchange reaction between the components of the stable pair.

The absence of complex-formation in this reciprocal system confirms, as was shown in the beginning of the present work, the tendency toward the weakening of complex-formation in reciprocal systems of the chloride-sulfate series of mono- and divalent metals in the systematic replacement of sodium and lithium by potassium.

According to the value for the conditional thermal effect of the reaction of exchange, calculated from the heat of formation of the salts as 1.58 kcal/gram-equivalent, this system should be reversible-reciprocal [10]; this, however, is not confirmed by its space diagram, which corresponds to the irreversible-reciprocal type.

Such a sharp lack of correspondence between the thermal effect of the reaction of exchange in a reciprocal system, and the character of its diagram indicates that: 1) either the conditional thermal effect of the exchange reaction, with small values for the thermal effect, is not always applicable for a priori judgment of the character of the reciprocal system, or 2) the available literature data on the heat of formation of some salts are not completely accurate.

SUMMARY

1. The reciprocal system Li, Ca || Cl, SO_4, which has been studied by the visual-polythermal method, is an irreversible-reciprocal system without complex-formation and has two triple eutectic points.

2. The absence of complex-formation in the system confirms the previously noted weakening of the tendency toward complex-formation in systems of the chloride-sulfate series of mono- di valent metals on the replacement of lithium and sodium by potassium, with one and the same divalent metal.

3. The lack of correspondence between the conditionally calculated thermal effect of the exchange reaction in the system and the character of its space diagram has been established.

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PHYSICO-CHEMICAL INVESTIGATION OF AQUEOUS DIOXANE SOLUTIONS

VI. DIOXANE SOLUTIONS OF HYDROGEN CHLORIDE

Ya. F. Mezhennyi

Kablukov [1], studying solutions of hydrogen chloride in solvents of different dielectric constants, established the existence of a dependence relationship between the electroconductivity and the dielectric constant of the medium (Kablukov's rule). Starting from Kablukov's rule it is possible to predict very small values for the electroconductivity of solutions of HCl in dioxane. The value for the electroconductivity should be less, for corresponding concentrations than that obtained by Kablukov for an ethereal solution of hydrogen chloride, and should approximate those obtained for benzene solutions of HCl.

1. Solubility of Hydrogen Chloride in Dioxane

The method of preparation and the properties of the dioxane utilized in these experiments have been described previously [2]. The hydrogen chloride was prepared by the interaction of sulfuric acid and chemically pure sodium chloride; it was dried with sulfuric acid.

The experiments showed that dry hydrogen chloride is very soluble in dioxane, completely colorless, transparent solutions being formed. As in the case of water, the process of solution of gaseous hydrogen chloride in dioxane is accompanied by the evolution of a considerable quantity of heat.

The determination of the solubility was carried out by the saturation of a weighed portion of dioxane (which had been placed in a thermostat) with hydrogen chloride until the weight was constant. It was established that the concentration of hydrogen chloride in a saturated solution at 20° was equal to 45.0 mole %, and the concentration of a saturated solution at 12° was 52.3 mole %.

In addition to the determination by the gravimetric method, the concentration of hydrogen chloride was also determined by the volumetric method, for which individual weighed portions of the solution were added to water in a calibrated flask up to 50 ml and titrated with a solution of sodium hydroxide in the presence of phenolphthalein. The quantity of hydrogen chloride in the dioxane solution, obtained by the volumetric method, coincided with the quantity of HCl found by gravimetric means.

2. Electroconductivity of Solutions of Hydrogen Chloride in Dioxane

The determination of the electroconductivity was carried out on an assembly with a metrically calibrated rheochord and telephone. The apparatus was supplied with power by a tube generator of audible frequency. An air condenser of variable capacity was connected in parallel with the resistance box. The vessel for the measurement of the electroconductivity consisted of a small cylinder with rigidly soldered platinum-plated platinum electrodes. In order to prevent the evaporation of the solutions and the falling of moisture into them, the vessel was closed with a ground-glass stopper with an elongated polished section. The length of the polished section was 2.5 cm. Besides being sealed with a ground-in cover, the vessel was closed with a dry rubber cap. The calibration of the vessel was carried out by means of an aqueous potassium chloride solution. The data obtained on the electroconductivity of dioxane solutions of hydrogen chloride are given below.

TABLE 1

Electroconductivity of solutions of hydrogen chloride in dioxane at 20°

c(gram-equivalent/ liter)	v(liter/gram-equivalent)	κ	$\lambda \cdot 10^{-3}$
0	–	$< 10^{-8}$	–
3.343	0.290	$< 10^{-8}$	–
5.610	0.178	$< 10^{-8}$	–
7.670	0.133	$2.52 \cdot 10^{-6}$	0.336
7.740	0.129	$5.26 \cdot 10^{-6}$	0.673

As is evident from the data given in Table 1, hydrogen chloride, while a strong electrolyte in aqueous solutions, is by no means a strong electrolyte on its dissolution in dioxane, its dielectric constant in the latter case being 36 times less than in the case of its dissolution in water. From the data of Table 1 it is evident that in dioxane solutions with a concentration of 3.34 N, and even of 5.61 N, the electroconductivity of this system differs by only a small amount from the electroconductivity of pure distilled water. Only beginning with 7.67 N (which corresponds to 43.2 mole % HCl) does the specific electroconductivity reach a magnitude of the order of a millionth part, and the equivalent electroconductivity reach a magnitude of the order of a ten-thousandth part, of the order of the electroconductivity of distilled water. At the same time, for aqueous solutions of HCl, at these concentrations the specific electroconductivity reaches values of the order of 0.7 and the equivalent electroconductivity reaches values of about 150 reciprocal ohms. Therefore, in regard to electroconductivity, solutions of hydrogen chloride in dioxane are thousands of times weaker than even such weak electrolytes in water as acetic acid; the equivalent electroconductivity of the latter, at a concentration of 5 g-mole/liter in water, is 0.28; HCl in dioxane has an electroconductivity of only $0.3 \cdot 10^{-9}$ reciprocal ohms.

One more fact attracts our attention. As is evident from the data of Table 1, the equivalent electroconductivity of hydrogen chloride in dioxane increases with the concentration, and therefore, falls upon dilution. In other words, we have here a typical "anomalous curve" $\lambda = f(v)$.

3. Cryoscopy of Dioxane Solutions of Hydrogen Chloride

It is evident from the data of the investigation of the electroconductivity of solutions of hydrogen chloride in dioxane, that this solution dissociates only very slightly, and that hydrogen chloride in dioxane, unlike the case of its solutions in water, is a very, very weak electrolyte, or even a non-electrolyte.

In connection with the practically negligible dissociation of the hydrogen chloride molecules it was interesting to establish its molecular weight in dioxane; for this purpose, cryoscopic methods were used, giving, as is known, for aqueous solutions of HCl $\Delta t_{experimental} > \Delta t_{theoretical}$; $M_{experimental} < M_{theoretical}$. Starting from the data on the electroconductivity of HCl, in dioxane, one might expect in this case that $M_{experimental} > M_{theoretical}$.

The systems for the cryoscopic measurements were prepared in the following way. First, the temperature of crystallization of pure dioxane was determined in the cryoscopic apparatus; then a definite quantity of a previously prepared dioxane solution of hydrogen chloride, with a known HCl content, was introduced. Further changes in the ratio of the components of the solution were brought about by the addition of definite quantities of dioxane, as is evident from the first column of Table 2.

TABLE 2

Determination of the molecular weight of hydrogen chloride in dioxane by the cryoscopic method

Expt. No.	Weight of dioxane G (in g)	Dissolved HCl g (in g)	Lowering of the temperature of crystallization $\Delta t_{expt.}$	$M_{expt.} = 4.83 \cdot \frac{1000 \cdot g}{\Delta t_{expt.} \cdot G}$	$x = \frac{M_{expt.}}{M_{theo.}}$
1	6.420	0	0.00	–	–
2	6.431	0.3489	6.32	41.5	1.15
3	7.383	0.3489	5.50	41.7	1.13
4	8.344	0.3489	4.91	40.8	1.11
5	10.693	0.3489	3.69	42.6	1.158
6	12.651	0.3489	3.11	42.9	1.163
7	13.481	0.3489	2.82	46.3	1.25
8	15.224	0.3489	2.44	46.1	1.25
9	16.235	0.3489	2.17	49.4	1.34
10	17.359	0.3489	2.20	54.06	1.46
11	19.286	0.3489	2.25	39.2	1.07
12	21.218	0.3489	1.76	45.1	1.23
13	5.31	0.3489	0.00	–	–
14	5.779	0.0731	1.43	42.5	1.16
15	6.749	0.0731	1.22	42.8	1.17
16	7.090	0.0731	0.99	50.3	1.37
17	7.531	0.0731	0.92	50.3	1.37

It is evident from the data of Table 2 that in all the investigated cases in the interval of the depression of the freezing point up to 6.32° (which corresponds to concentrations of up to 1000 mole of hydrogen chloride per 1.5 g of dioxane), the molecular weight of HCl proved to be higher than the theoretical value.

This can be explained either by the partial association of the hydrogen chloride molecules according to the equation

$$xHCl \rightleftharpoons (HCl)x, \quad (1)$$

or by the formation of complex ions through the combing of ions with undissociated molecules:

$$HCl \rightleftharpoons H^{\cdot} + Cl' \quad (2)$$

$$H^{\cdot} + HCl \rightleftharpoons H_2^{\cdot}Cl \quad (3)$$

$$Cl' + HCl \rightleftharpoons HCl_2' \quad (4)$$

or, summarizing,

$$3HCl \rightleftharpoons H_2^{\cdot}Cl + HCl_2'. \quad (5)$$

If, however, we assume the association of neutral molecules, even if only three of them, equations (1, 2, 3) may be represented by the equation:

$$(HCl)_3 \rightleftharpoons H_2^{\cdot}Cl + HCl_2'. \quad (6)$$

If the equilibrium took place according to equation (2), corresponding to an aqueous solution of hydrogen chloride, then we would have the case $M_{experimental} < M_{theoret.}$ and $\Delta t_{experimental} > \Delta t_{theoretical}$. In view of the fact that the molecular weight, according to cryoscopic data, turns out to be greater than the theoretical, there is no basis for assuming the scheme of simple dissociation (equation 2) and the presence, in a dioxane solution of hydrogen chloride, of the simple ions $H^{\cdot}$ and Cl'.

Nor is there any basis for considering that the state of the dissolved molecules of hydrogen chloride is described only by the equilibrium represented by equation (1), even if it is shifted strongly to the left (monomeric molecules), since this would disagree with the data on the electroconductivity of this system. Although the value for the electroconductivity is insignificant in absolute terms, its relative magnitude is, nevertheless, observed; therefore, it is most probable that the equilibrium in this system conforms to equations (1, 5, 6).

TABLE 3

Thermal analysis of the system hydrogen chloride – dioxane

HCl (in mole %)	Crystallization temperature
0	11.7°
3.78	9.9
4.14	9.5
4.55	9.5
4.75	9.53
5.2	9.0
5.8	8.2
7.2	7.6
9.0	6.4
10.1	5.8
11.5	5.0

4. Thermal Analysis of the System Hydrogen Chloride – Dioxane

We investigated only that branch of the curve embracing the comparatively small interval of hydrogen chloride concentration represented in Table 3.

From the data of Table 3 it is evident that the addition of increasing quantities of hydrogen chloride to the dioxane depresses the crystallization temperature of the solution more and more, the depression of the freezing point of a solution of HCl in dioxane in the investigated region (up to 11 mole % HCl), having almost a linear character.

5. Comparison of the Conductivity of Solutions of Hydrogen Chloride in Dioxane and in other Solvents

Uniting our data with the results of Kablukov's investigations, we obtain the picture presented in Table 4.

TABLE 4

Electroconductivity of solutions of hydrogen chloride in various solvents

Solvent	Dielectric constant ε	Dilution (l/mole)	λ	Investigator
Dioxane	2	0.29	A trace	The author
		0.178	the same	
		0.133	0.0003	
		0.129	0.000673	
Benzene	2.29	–	A trace	I. A. Kablukov [3]
Ethyl ether	4.37	3.52	0.00004	
Ethyl alcohol	25.4	100	27.17	
Methyl alcohol	35.4	91.16	117.06	
Water	81	100	394	

As we see from the data of Table 4, our data, in full agreement with that of Kablukov, again confirms the great importance of the ϵ of the medium, both as a factor changing the strength of an electrolyte, and as a factor converting a strong electrolyte in an aqueous medium into a weak electrolyte in alcohol, a very weak electrolyte in ether, and almost into a non-electrolyte in dioxane and benzene.

SUMMARY

1. Hydrogen chloride is very soluble in dioxane, since at 20° its content in the system can reach 45 mole %, and at 12° it can even reach 52 mole %. The dissolution of hydrogen chloride in dioxane is an exothermic process and is accompanied by the evolution of a considerable quantity of heat.

2. The equivalent electroconductivity of dilute solutions of HCl in dioxane $< 10^{-7}$ reciprocal ohms; only with $c \approx 7$ gram-equivalents/liter does it reach values of the order of 10^{-4} which is a million times less than the electroconductivity of HCl in aqueous solutions. The equivalent electroconductivity of hydrogen chloride in dioxane falls with dilution.

3. It has been shown by cryoscopic means that unlike aqueous solutions of HCl, the observed molecular weight of hydrogen chloride in dioxane is greater than the theoretical value. In accordance with the data on electroconductivity, this causes us to recognize the presence of polymerization (association) of hydrogen chloride molecules in dioxane solutions.

4. The composition – melting point curve of the system dioxane – hydrogen chloride, has been investigated from pure dioxane, up to the system containing about 12 mole % HCl. The almost linear character of this curve for the investigated region has been shown.

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THE MOLECULAR HEAT CAPACITY OF ORGANIC COMPOUNDS OF VARIOUS DEGREES OF HYDROGENATION

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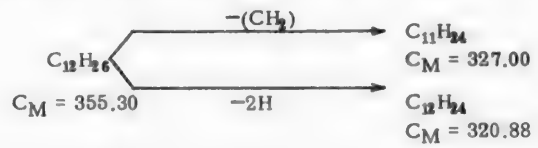
In one of my previous papers [1], I have shown that among the values for the molecular heat capacity of liquid hydrocarbons of various degrees of hydrogenation there exists a certain periodicity. Attention was attracted to the fact that the decrease in molecular heat capacity after the dehydrogenation of saturated hydrocarbons to mono-unsaturated hydrocarbons is a more or less constant value. Further dehydrogenation, however, evidently leads to a more rigid molecular structure, and, as a consequence of this, the heat capacity of the substance is lowered more sharply. This alone indicates new possibilities for the evaluation of the character of the structure of hydrocarbon molecules by means of the measurement of the heat capacity of these molecules. For ethane it turned out to be possible [2] to use another method, namely, the comparison of the calculated and measured heat capacity, which unconditionally revealed the entire picture of the structure and energy state of the molecule. This method is not applicable to more complicated molecules, since it would be impossible to take into account all the frequencies of natural oscillation in this case, and therefore the use of quantum formulas for the calculation of the heat capacity would also be impossible. Therefore, the utilization of the heat capacity as one of the criteria for the evaluation of the structure and energetics of complex molecules cannot be applied in all cases; it turns out that the most useful method for their utilization is the measurement of the heat capacity of substances whose structures are comparable.

From this point of view, in the present communication we have examined new cases of changes in the molecular heat capacity of organic compounds of various degrees of hydrogenation, and we have made more precise the various hypotheses expressed in the preceding paper. On the investigation of the heat capacity of the heavier liquid hydrocarbons, beginning with C_{10} and higher, it turned out that ΔC_M reaches values above 30, which essentially completes the table.

	Hydrocarbons					
	$C_{12}H_{26}$	$C_{12}H_{24}$	$C_{13}H_{28}$	$C_{13}H_{26}$	$C_{14}H_{30}$	$C_{14}H_{28}$
Magnitudes of the molecular heat capacity	355	321	385	347	402	372
ΔC_M	34		38		30	

Thus, the dehydrogenation of hydrocarbons, with the elimination of only two hydrogen atoms, lessens the molecular heat capacity to a greater extent than the transition to the next lower homolog. For example:



ΔC_M varies, however, within wide limits, for the value of the molecular heat capacity of various organic compounds. For oxygen-containing compounds, it is, as a rule, lower for high-molecular compounds, and, on the other hand, higher for low-molecular compounds:

$$\underset{C_M = 273.62}{C_4H_9-COOCH_2-CH_2-CH_3} \xrightarrow{-2H} \underset{C_M = 267.95}{C_4H_9COOCH_2-CH=CH_2} \quad \Delta C_M = 5.67$$

$$C_3H_7-COOC_3H_7 \xrightarrow{-2H} C_3H_7-COOC_3H_5$$
$$C_M = 249.73 \qquad C_M = 241.53 \quad \Delta C_M = 8.20$$

$$CH_3COOC_3H_7 \xrightarrow{-2H} CH_3COOC_3H_5$$
$$C_M = 195.94 \qquad C_M = 180.20 \quad \Delta C_M = 15.74$$

$$C_3H_7OOC-COOC_3H_7 \xrightarrow{-4H} C_3H_5OOC-COOC_3H_5$$
$$C_M = 315.29 \qquad C_M = 303.11 \quad \Delta C_M = 12.18$$

The heat capacity of the esters of benzoic acid occupies a special place:

$$C_6H_5COOC_3H_7 \xrightarrow{-2H} C_6H_5COOC_3H_5$$
$$C_M = 273.22 \qquad C_M = 263.09 \quad \Delta C_M = 10.13$$

The examples which have been given indicate that the double bond which appears as a result of dehydrogenation leaves its imprint on the whole molecule, lowering both the number of oscillators and the amplitude of natural oscillations, i. e., it gives to the molecule rigidity of structure. If the molecule by itself has a sufficiently rigid structure, and it is therefore impossible to lower sharply the number of oscillators in it by the introduction of a double bond, the fall in its heat capacity on dehydrogenation is insignificant:

$$C_6H_5-CH_2-CH_2-CH_3 \xrightarrow{-2H} C_6H_5-CH-CH=CH_2$$
$$C_M = 200.88 \qquad C_M = 193.99 \quad \Delta C_M = 6.89$$

Especially interesting is the comparison of the heat capacity of those substances whose chemical structure is basically changed upon dehydrogenation. We will examine three cases of dehydrogenation of this type.

1. Dehydrogenation of Ethane

$$H_3C-CH_3 \xrightarrow{-2H} H_2C=CH_2 \xrightarrow{-2H} HC\equiv CH$$
$$C_M = 48.55 \qquad C_M = 42.14 \qquad C_M = 41.72$$
$$\Delta C_M = 6.41 \qquad \Delta C_M = 0.42$$

The step by step dehydrogenation of ethane to ethylene and then to acetylene leads to the above picture.

2. Dehydrogenation of n-Hexane

$$C_2H_5-CH_2-CH_2-CH_2-CH_3 \rightarrow C_2H_5-CH_2-CH_2-CH=CH_2 \rightarrow C_2H_5-CH=CH-CH=CH_2$$
$$C_M = 189.63 \qquad C_M = 177.81 \qquad C_M = 150.00$$
$$\Delta C_M = 11.82 \qquad \Delta C_M = 27.81$$

Here the fall in the molecular heat capacity takes place over both steps of dehydrogenation, the fall being sharper in the second step.

3. Dehydrogenation of Cyclohexane

$C_M = 176.00 \qquad C_M = 100.41 \qquad C_M = 134.00$
$\Delta C_M = 75.59 \qquad + \Delta C_M = 33.59$

In this case the dehydrogenation in the first step leads to a sharp lowering of the molecular heat capacity.* In the second step, on the other hand, dehydrogenation leads to an increase in the molecular heat capacity.

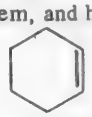
All three cases, showing one and the same process of dehydrogenation, indicate, however, three different directions of the change of molecular heat capacity. The exceptional disproportion of these changes indicates very

* Dehydrogenation of n-hexane to hexadiene lowers the molecular heat capacity only by 39.63 Joules/moles degrees, while here it is lowered by 75.59.

clearly that the loss of molecular heat capacity takes place here least of all on account of the loss of hydrogen, and, therefore, of the decrease in the number of CH-oscillators in the molecule. The chief cause of the change is undoubtedly connected with the structure and energy state of the molecule.

The great difference between the heat capacity of ethane and ethylene is explained by the loss of torsion vibration (or free rotation) of the methyl groups on the dehydrogenation of ethane, as was shown by Teller and Weigert [2]. Further dehydrogenation did not show any essential influence on the character of the natural oscillations of the molecule, and therefore the insignificant difference between the molecular heat capacities of ethylene and acetylene is explained no more as the loss of two CH-oscillators.

The progressive loss of molecular heat capacity on the dehydrogenation of n-hexane occurs as a consequence of the fact that the formation of each new double bond makes the structure of the molecule less and less mobile. It is also fully evident that at 20° in normal hexane, hexene, and hexadiene, the free rotation of radical groups around the axis of the C–C bond is absent. The most convincing proof of this is the comparison of the molecular heat capacity of hexene, cyclohexane, representing a closed system, and hexadiene.

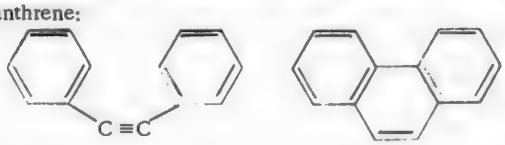


$C_4H_9-CH=CH_2$ $C_2H_5-CH=CH-CH=CH_2$

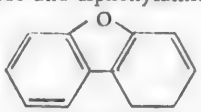
$C_M = 177.81$ $C_M = 176.00$ $C_M = 150.00$

But most interesting is the raising of the molecular heat capacity on the dehydrogenation of cyclohexadiene to benzene. In spite of the loss of two hydrogen atoms, and, therefore, the apparent lowering of the number of oscillators, the molecular heat capacity of benzene turns out to be greater than that of cyclohexadiene; this indicates that the aromatic ring has a less rigid and taut structure than the unsaturated cyclic compounds.

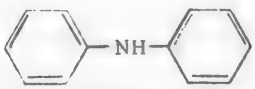
The measured molecular heat capacity can also be used for the determination of whether, in a given molecule, torsion oscillation or free rotation along the C–C axis takes place, as in the case of ethane. For this purpose it is necessary to compare the molecular heat capacities of open and closed systems having the same number of oscillators, for example, tolane and phenanthrene:



each of which contains 4 non-hydrogenated atoms and 10 CH-groups. There is, as yet, no data on the heat capacity of these particular substances. However, the heat capacity has been measured (at 30 and 50°, respectively, for the liquid state) of diphenyl oxide and diphenylamine.



$C_M = 280.56$



$C_M = 292.44$ $\Delta C_M = 11.88$

The comparison of the data on these two compounds confirms the existence of torsion oscillation of the nuclei in diphenylamine, and the relative rigidity of the closed system of diphenyl oxide.

SUMMARY

Additional data has been presented indicating the possibility of the use of the measured heat capacity of organic compounds for the evaluation of the structure and natural oscillations of molecules.

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DERIVATIVES OF ACETYLENE

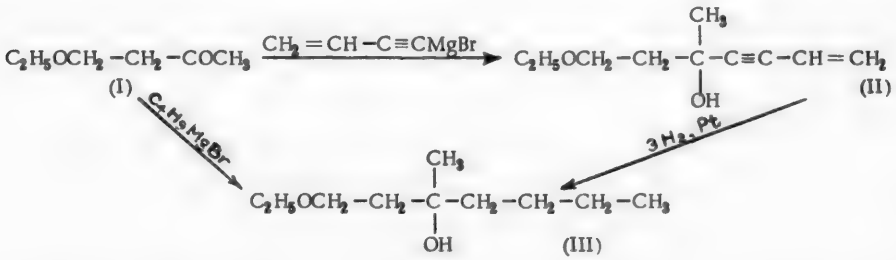
161. SYNTHESIS AND TRANSFORMATIONS OF METHYL-β-ETHOXYETHYLVINYLETHINYLCARBINOL

I. N. Nazarov, S. A. Vartanyan, and V. N. Zhamagortsyan

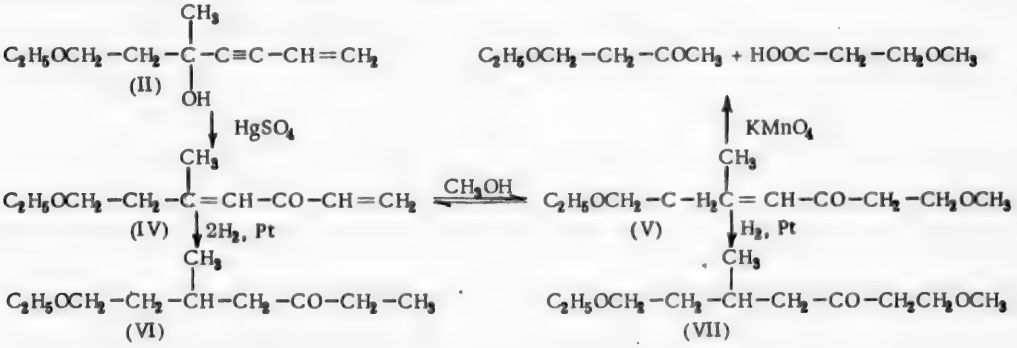
In our preceding work we described the synthesis and transformations of vinylethinylcarbinols containing methoxy groups [1]. It was of interest to explain the possibility of the synthesis of methyl-β-ethoxyethylvinylethinylcarbinol and to study its transformations for the purpose of clarifying the influence of the ethoxy group on the chemical activity of this carbinol.

Unlike aliphatic [2], alicyclic [3], and heterocyclic [4] ketones, methyl-β-ethoxyethyl ketone (I) proved to be completely incapable of entering into a condensation reaction with vinylacetylene in the presence of powdered potassium hydroxide; along with this, similar to other β-alkoxy ketones [5], it thickened completely into a sticky, non-distillable mass.

The synthesis of the carbinol (II) was carried out by us through the use of an organometallic compound. Upon the action of magnesium bromovinylacetylene on methyl-β-ethoxyethyl ketone (I), which was obtained by the hydration of vinyl acetylene in ethyl alcohol, methyl-β-ethoxyethylvinylethinylcarbinol (II) was obtained in a yield of about 90%.

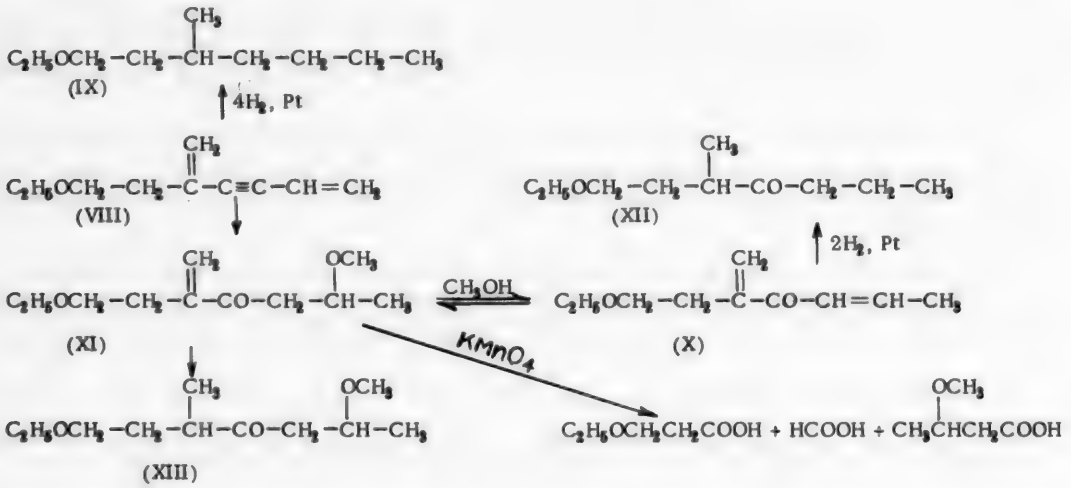


Upon the hydrogenation of the carbinol (II) with a platinum catalyst, three molecules of hydrogen are absorbed and methyl-β-methoxyethylbutylcarbinol (III) is formed. The latter was also obtained with a yield of 50% by the action of butyl magnesium bromide on the ethoxy ketone (I). Under the influence of a methanol solution of mercuric sulfate, the carbinol (II), like other vinylethinylcarbinols, is easily isomerized to 5-methyl-7-ethoxy-1,4-heptadien-3-one (IV), which in the conditions of the experiment, adds one molecule of methanol on the unsubstituted vinyl group, and forms 5-methyl-1-methoxy-7-ethoxy-4-hepten-3-one (V). The free divinyl ketone (IV) is obtained with difficulty on the vacuum distillation of the unsaturated alkoxy ketone (V) in the presence of para-toluenesulfonic acid; in this case, only the methoxy group, which is in the β-position in relation to the carbonyl, is split off, while the ethoxy group in the γ-position remains unchanged.



Upon hydrogenation with a platinum catalyst, the divinyl ketone (IV) takes up two molecules of hydrogen and is transformed into 5-methyl-7-ethoxyheptan-3-one (VI); the analogous hydrogenation of the unsaturated methoxy ketone (V) leads to the taking up of one molecule of hydrogen and gives 5-methyl-1-methoxy-7-ethoxyheptan-3-one (VII). The structure of the methoxy ketone (V) was definitely established through the use of oxidation; upon oxidation, methyl-β-ethoxyethyl ketone (I) and β-methoxypropionic acid were obtained.

β-Ethoxyvinylethinylcarbinol (II) dehydrates easily on treatment with 50% sulfuric acid at 60° for 1.5 hours; it gives a mixture of dienes which is mainly 2-β-ethoxyethyl-1,5-hexadien-3-yne (VIII). Apparently the β-ethoxyethyl radical is involved in the dehydration of the carbinol (II) to only an insignificant degree. Upon hydrogenation in an alcoholic solution in the presence of a platinum catalyst, the dienyne (VIII) takes up four molecules of hydrogen and is converted into 3-methyl-1-ethoxyheptane (IX).



The dienyne (VIII) was hydrated in aqueous methanol solution in the presence of mercuric sulfate for 25 hours at 63°; thereupon, 2-β-ethoxyethyl-1,4-hexadien-3-one (X) was formed, which, under the conditions of the experiment adds one molecule of methanol at the propenyl radical and is completely converted into 5-methoxy-2-β-ethoxyethyl-1-hexen-3-one (XI). Upon the vacuum distillation of the dialkoxy ketone (XI) in the presence of para-toluenesulfonic acid, 2-β-ethoxyethyl-1,4-hexadien-3-one (X) is obtained. Upon hydrogenation, the ethoxydienone (X) takes up two molecules of hydrogen and is converted into 3-methyl-1-ethoxyheptan-4-one (XII); the dialkoxy ketone (XI) upon hydrogenation takes up one molecule of hydrogen and gives 5-methyl-2-methoxy-7-ethoxyheptan-4-one (XIII).

Upon the oxidation of the dialkoxy ketone (XI) with permanganate, formic, β-ethoxypropionic, and β-methoxybutyric acids were obtained; this confirms the structure attributed to this compound.

EXPERIMENTAL

Synthesis of methyl-β-ethoxyethylvinylethinylcarbinol (II). A solution of magnesium ethyl bromide was prepared in a 2 liter round-bottomed flask, equipped with a mechanical stirrer, a dropping funnel, and a reflux condenser; the materials used were 70 g of magnesium and 330 g of ethyl bromide in 600 ml of anhydrous ether. 200 g of gaseous vinylacetylene was passed through the ether solution of magnesium ethyl bromide for 2.5 hours with cooling down to −18°, and the reaction mixture was allowed to stand overnight. Then the reaction mixture was stirred for one hour at room temperature and for 40 minutes at the boiling point of the ether, until the evolution of ethane had ceased completely. 230 g of methyl-β-ethoxyethyl ketone was added by drops over the course of 6 hours to the magnesium bromovinylacetylene which was obtained. During the time of the addition of the ketone, the temperature of the reaction mixture varied between −18 and +5°. The following day the reaction mixture was stirred for one hour at room temperature and for 40 minutes at the boiling point of the ether. The reaction product was hydrolyzed with 10% hydrochloric acid (1060 ml) while being cooled with ice water. The ether layer was separated, the product was neutralized with a 5% soda solution, washed with water, and dried with sodium sulfate. After the distillation of the ether, 300 g of methyl-β-ethoxyethylvinylethinylcarbinol was obtained.

B. p. 88-90° at 4 mm, d_4^{20} 0.9260, n_D^{20} 1.4740, MR_D 51.00; calc. 49.08.

Found %: C 71.37, 71.10; H 9.95, 9.77. $C_{10}H_{16}O_2$. Calculated %: C 71.42; H 9.52.

The obtained carbinol was a colorless, mobile liquid with a characteristic odor; upon being allowed to stand without a stabilizer, it thickens and is converted into a yellow glass-like polymer.

Hydrogenation of methyl-β-ethoxyethylvinylethinylcarbinol. 3 g of the freshly-distilled carbinol (II) in 10 ml of ethyl alcohol was hydrogenated in the presence of a platinum catalyst. The volume of hydrogen taken up was 1.3 l (calculated 1.21 l). 2.3 g of methyl-β-ethoxyethylbutylcarbinol (III) was obtained in the form of a colorless liquid with a pleasant odor.

B. p. 85° at 5 mm, d_4^{20} 0.8690, n_D^{20} 1.4350, MR_D 52.23; calc. 51.55.

Found %: C 69.02, 68.85; H 12.85, 12.88. $C_{10}H_{22}O_2$. Calculated %: C 68.95; H 12.64.

The action of butyl magnesium bromide on methyl-β-ethoxyethyl ketone (I). The butyl magnesium bromide was prepared in the usual manner from 15 g of butyl bromide and 2.6 g of magnesium in 60 ml of anhydrous ether. Then, 12 g of methyl-β-ethoxyethyl ketone was added by drops, over the course of an hour, with cooling to 0° and constant stirring. The stirring was continued for another hour at room temperature and for 30 minutes at the boiling point of the ether. The reaction product was hydrolyzed with 10% hydrochloric acid (40 ml) upon cooling with water. The ether layer was separated, neutralized with a 5% soda solution, washed with water and dried with sodium sulfate. After the driving off of the ether, the residue was vacuum distilled; 9.3 g of the above-described methyl-β-ethoxyethylbutylcarbinol (III) was obtained.

B. p. 93-94° at 10 mm, d_4^{20} 0.8755, n_D^{20} 1.4360.

Isomerization of methyl-β-ethoxyethylvinylethinylcarbinol (II). A mixture of 41 g of the freshly-distilled carbinol (II) which had been stabilized with pyrogallol, 120 g of distilled methanol, and 2 g of finely-ground mercuric sulfate were mixed and heated for 8 hours. In the beginning of the reaction, the temperature was raised to 55°, then the temperature rose, due to the heat of the reaction, to 59°, and then it fell slowly and was kept at 40°. Over this period of time 4 more g of mercuric sulfate was added in portions. The reaction product was decanted with the catalyst; the main part of the methanol was evaporated over a water bath in a low vacuum at 40°. The reaction product was carefully neutralized with soda, extracted with ether, washed with water, and dried with sodium sulfate. After the ether was distilled off and the product was vacuum distilled, 38.5 g of 5-methyl-1-methoxy-7-ethoxy-4-hepten-3-one (V) was obtained.

B. p. 108-109° at 2 mm, d_4^{20} 0.9613, n_D^{20} 1.4640, MR_D 57.40; calc. 55.83.

Found %: C 65.83, 65.57; H 10.27, 10.15. $C_{11}H_{20}O_3$. Calculated %: C 66.00; H 10.00.

Hydrogenation of 5-methyl-1-methoxy-7-ethoxy-4-hepten-3-one (V). 2.9 g of the freshly-distilled alkoxy ketone (V) was hydrogenated in 10 ml of ethanol in the presence of a platinum catalyst. 0.4 liter of hydrogen was taken up instead of the 0.348 liter which was calculated. 2.2 g 5-methyl-1-methoxy-7-ethoxy-heptan-3-one (VII) was obtained.

B. p. 98-99° at 2 mm, d_4^{20} 0.9302, n_D^{20} 1.4380; MR_D 57.01; calc. 56.30.

Found %: C 65.03, 65.32; H 11.03, 11.15. $C_{11}H_{22}O_3$. Calculated %: C 65.34; H 10.89.

Oxidation of 5-methyl-1-methoxy-7-ethoxy-4-hepten-3-one (V). 11 g of the ketone (V) was mixed with 200 ml of water, and 27 g of finely-ground potassium permanganate was added to the mixture, with constant stirring over the course of 5 hours; after the addition of the potassium permanganate, the reaction mixture was allowed to stand overnight. On the following day the product was filtered, the manganese dioxide was washed twice with hot water, the neutral product was extracted from the filtrate with ether, and the ether solution was dried with sodium sulfate and distilled. 1.3 g of methylethoxyethyl ketone with a boiling point of 145-147° at 680 mm, n_D^{20} 1.4096 was obtained. The 2,4-dinitrophenylhydrazone of the obtained ketone melted at 100-101° and did not give a depression upon being mixed with a known sample.

The aqueous solution of the organic acids was evaporated until dry over a water bath, the residue was acidified with concentrated hydrochloric acid, extracted with ether, and the ether solution was dried with sodium sulfate and vacuum distilled. The product was 3.7 g of β-methoxypropionic acid with a boiling point of 103-105° at 11 mm; 199-203° at 680 mm, n_D^{20} 1.4201.

The splitting off of methanol from 5-methyl-1-methoxy-7-ethoxy-4-hepten – 3-one (V). 22.5 g of the ketone (V), 0.005 g of pyrogallol, and 0.5 g of para-toluenesulfonic acid were heated for 20 minutes over a metallic bath at 100° and at a pressure of 25 mm. Then 13 g of a substance with a boiling point of 88-90° at a pressure of 7 mm was distilled off. After two distillations, 7 g of 5-methyl-7-ethoxy-1,4-heptadien- 3-one (IV) was obtained.

B. p. 71-72° at 2 mm, d_4^{20} 0.9285, n_D^{20} 1.4770, MR_D 51.17; calc. 49.10.

Found %: C 71.32, 71.02; H 9.93, 9.60. $C_{10}H_{16}O_2$. Calculated %: C 71.43; H 9.52.

The obtained dienone (IV) is a yellowish, mobile liquid with a characteristic odor. On standing without a stabilizer it quickly thickens, forming a transparent solid polymer that is light yellow in color.

Hydrogenation of 5-methyl-7-ethoxy-1,4-heptadien- 3-one (IV). 3.5 g of the freshly-distilled ketone was hydrogenated in 10 ml of ethanol in the presence of a platinum catalyst. The quantity of hydrogen taken up was 1.1 liter; 1 liter of hydrogen is required for the hydrogenation of two double bonds. 2.8 g of 5-methyl-7-ethoxy-heptan-3-one (VI) was obtained in the form of a colorless, mobile liquid with a pleasant odor.

B. p. 68-69° at 3 mm, d_4^{20} 0.8827, n_D^{20} 1.4310, MR_D 50.45; calc. 50.03.

Found %: C 69.19, 68.90; H 12.27, 12.00. $C_{10}H_{20}O_2$. Calculated %: C 69.76; H 11.63.

Dehydration of methyl-β-ethoxyethylvinylethinylcarbinol (II). A mixture of 149 g of the carbinol (II), 0.005 g of pyrogallol, and 149 g of 50% sulfuric acid was heated, with constant stirring, over a water bath at 60° for one hour and 20 minutes. At the beginning of the reaction, a rise in temperature was noted (up to 73°). The reaction product was extracted with ether, neutralized with soda, washed with water, dried with sodium sulfate, and vacuum distilled. 80 g of 2-β-ethoxyethyl-1,5-hexadien-3-yne (VIII) was obtained.

B. p. 67-69° at 4 mm, d_4^{20} 0.8636, n_D^{20} 1.4970, MR_D 50.82; calc. 47.09.

Found %: C 80.41, 79.45; H 9.63, 9.33. $C_{10}H_{14}O$. Calculated %: C 80.0; H 9.33.

The obtained dienyne (VIII) is a colorless, mobile liquid; upon standing without a stabilizer it quickly polymerizes, forming a thick, glass-like polymer that is yellow in color.

Hydrogenation of 2-β-Ethoxyethyl-1,5-hexadien-3-yne (VIII). 3.2 g of freshly distilled dienyne (VIII) was hydrogenated in the presence of a Pt catalyst in 10 ml of ethyl alcohol. 2.1 liters of hydrogen was absorbed instead of the calculated 2.048 liters. We isolated 2.3 g of 3-methyl-1-ethoxyheptane (IX) in the form of a colorless, transparent liquid with a pleasant odor.

B. p. 88° at 33 mm, d_4^{20} 0.7829, n_D^{20} 1.4130, MR_D 50.34; calc. 50.02.

Found %: C 76.17, 76.46; H 13.90, 13.94. $C_{10}H_{22}O$. Calculated %: C 75.95; H 13.92.

Hydration of 2-β-ethoxyethyl-1,5-hexadien-3-yne (VIII). 500 g of the dienyne (VIII), which had been stabilized with pyrogallol, was added by drops, with energetic stirring, to a boiling mixture of 2 g 90% methanol, 2 ml of concentrated sulfuric acid, and 136 g of mercuric sulfate. The reaction mixture was heated with stirring for 28 hours. In the course of this time, 36 additional g of mercuric sulfate was added to the mixture. The reaction product was filtered, the main part of the methanol was distilled off in a vacuum (70 mm) over a water bath at 45-50°. The residue was neutralized with soda, extracted with ether, washed with water, dried with sodium sulfate and vacuum distilled. 99 g of a mixture of the products of hydration was obtained; the mixture boiled between 110-128° at 6 mm. 79 g of the pure 5-methoxy- 2-β-ethoxyethyl-1-hexen - 3-one (XI) was isolated by means of repeated distillations.

B. p. 100-102° at 2 mm, d_4^{20} 0.9602, n_D^{20} 1.4550, MR_D 56.51; calc. 55.83.

Found %: C 65.55, 65.58; H 10.37, 10.29. $C_{11}H_{20}O_3$. Calculated %: C 66.00; H 10.00.

Hydrogenation of 5-methoxy-2-β-ethoxyethyl-1-hexen - 3-one (XI). 2.8 g of the freshly-distilled ketone was hydrogenated in 10 ml of ethyl alcohol in the presence of a platinum catalyst. 0.4 liter of hydrogen was taken up instead of the calculated 0.334 liter. 2.2 g of 5-methyl-2-methoxy-7-ethoxy-heptan - 4-one (XIII) was obtained.

B. p. 99-100° at 5 mm, d_4^{20} 0.9292, n_D^{20} 1.4366, MR_D 56.95; calc. 56.30.

Found %: C 65.48, 65.29; H 11.01, 11.31. $C_{11}H_{22}O_3$. Calculated %: C 65.35; H 10.89.

Oxidation of 5-methoxy-2-β-ethoxyethyl-1-hexen - 3-one (XI). 17 g of the ketone was mixed with 200 ml of water, and 43 g of finely-ground potassium permanganate was added over the course of 15 hours, with intense stirring and cooling with water. The manganese dioxide was filtered and washed twice with boiling water; from the filtrate, the neutralized product was extracted with ether, and dried with sodium sulfate. 2 g of the substance remained after the distilling off of the ether. The aqueous solution was evaporated over the water bath until dry, the residue of the salt was acidified with concentrated hydrochloric acid (13 ml), the organic acids were extracted with ether, dried with sodium sulfate, and vacuum distilled; there was 2.2 g of the first fraction boiling at 40-45° at 50 mm; the second fraction contained 5.1 g and boiled at 110-116° at 18 mm; there was 3 g of tarry residue.

The first fraction, which was formic acid (calomel test), after drying with roasted sodium sulfate, was distilled under normal pressure; b. p. 99-101° at 680 mm.

The second fraction is a mixture of β-methoxybutyric and β-ethoxypropionic acids. They were distilled once more under normal pressure; two new fractions were obtained. The first fraction is β-methoxybutyric acid with a b. p. of 200-203° at 670 mm, n_D^{20} 1.4205. Its silver salt was prepared.

Found %: Ag 48.45, 48.34. $C_5H_9O_3Ag$. Calculated %: Ag 48.0.

The second fraction was mainly β-ethoxypropionic acid with b. p. 206-209° at 670 mm, n_D^{20} 1.4625. Its silver salt was obtained.

Found %: Ag 48.06. $C_5H_9O_3Ag$. Calculated %: Ag 48.0.

The splitting off of methanol from 5-methoxy-2-β-ethoxyethyl-1-hexen - 3-one (XI). 17 g of the alkoxy ketone (XI), which had been stabilized with pyrogallol, was vacuum distilled in the presence of 0.052 g para-toluenesulfonic acid. At first the mixture was heated for 20 minutes over a metallic bath at a temperature of 100° and a pressure of 30 mm; then 11.3 g of a substance with a b. p. of 93-97° at 5 mm, n_D^{20} 1.4737 was distilled off. After distillation 9 g of 2-β-ethoxyethyl-1,4-hexadien - 3-one (X) was obtained.

B. p. 81-82° at 2 mm, d_4^{20} 0.9547, n_D^{20} 1.4760, MR_D 49.65; calc. 49.10.

Found %: C 70.23, 70.19; H 9.83, 9.52. $C_{10}H_{16}O_2$. Calculated %: C 71.47; H 9.52.

Hydrogenation of 2-β-ethoxyethyl-1,4-hexadien - 3-one (X). 2.7 g of the ketone (b. p. 90-92° at 4 mm, n_D^{20} 1.4750) was hydrogenated in a solution of 10 ml of ethanol in the presence of a platinum catalyst. 0.8 liter of hydrogen was taken up; 0.76 liter is required for the hydrogenation of two double bonds. 1.8 g of 1-ethoxy-3-methyl heptan - 4-one (XII) was obtained.

B. p. 74-75° at 4 mm, d_4^{20} 0.8996, n_D^{20} 1.4345, MR_D 49.88; calc. 50.03.

Found %: C 69.39, 69.44; H 11.34, 11.45. $C_{10}H_{20}O_2$. Calculated %: C 69.76; H 11.62.

SUMMARY

Methyl-β-ethoxyvinylethinylcarbinol (II) was obtained by the action of magnesiumbromovinylacetylene on methyl-β-ethoxyethyl ketone (I); under the influence of mercuric sulfate in a methanol solution, the methyl-β-ethoxyvinylethinylcarbinol (II) is isomerized to the divinyl ketone (IV). The latter, under the conditions of the experiment, adds methanol and gives the dialkoxy ketone (V).

The vinylethinylcarbinol (II), upon heating with 50% sulfuric acid, was converted into the dienyne (VIII); this in turn, on being heated in 90% methanol in the presence of mercuric sulfate, is hydrated to the dienone (X). This dienone, under the conditions of the experiment, adds methanol and gives the dialkoxy ketone (XI). Upon the splitting off of methanol from the dialkoxy ketone through the use of para-toluenesulfonic acid, the dienone (X) is again obtained. On the oxidation of the dialkoxy ketone with potassium permanganate, formic, β-ethoxypropionic, and β-methoxybutyric acids are obtained; this confirms the structure of the dienyne (VIII) and the ketone (XI).

Hydrogenation has been carried out, and the hydrogenated derivatives of the above described unsaturated compounds have been obtained.

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THE OBTAINING OF SOME HALOGEN DERIVATIVES BY THE ADDITION OF A HYDROGEN HALIDE TO UNSATURATED COMPOUNDS

N. N. Lebedev

The addition of hydrogen chloride to the double bond is one of the well known reactions which is catalyzed by aluminum chloride. It has acquired special importance for the industrial synthesis of ethyl chloride [1]. However, there are a great many cases in which this reaction is not used, since many halogen derivatives, especially those having secondary and tertiary chlorine atoms, are unstable in regard to the action of aluminum chloride, which decomposes them, the hydrogen halide being split off [2]:

$$R'CHCl-CH_2R \xrightarrow{AlCl_3} R'CH=CHR + HCl.$$

The olefin, in its turn, may be further polymerized under the action of aluminum chloride.

Thermodynamic calculations show that the above described reaction does not have to go to the right at ordinary temperatures. The factor which causes the shifting of the equilibrium is probably the tendency of the aluminum chloride to form complexes with the unsaturated compounds. The olefin which is formed combines with the catalyst, which causes the continuous shifting of the reaction in the direction of the decomposition of the halogen derivative.

It was found that this undesired reaction could be avoided by using a nitrobenzene solution of aluminum chloride as a catalyst. In the complex [3]

$$[(C_6H_5NO_2)_2AlCl_2]^+ [AlCl_4]^-$$

which is formed in the solution, the aluminum chloride is sufficiently strongly linked with the nitrobenzene, and cannot form complexes with the olefins; therefore, the decomposition of the halogen derivatives cannot take place in this case. Thus, we found that ethylidene chloride and methyl chloroform were fully stable in a nitrobenzene solution of aluminum chloride, while the latter, in the pure form, decomposed them very violently, with the giving off of a great deal of heat, and the splitting off of a hydrogen halide.

This opens up the possibility of obtaining a wide group of halogen derivatives by the convenient method of adding a hydrogen halide to an olefin or an olefin chloride in a nitrobenzene solution of aluminum chloride.

$$CH_2=CCl_2 + HCl \xrightarrow[C_6H_5NO_2]{AlCl_3} CH_3CCl_3.$$

This method is not limited to chlorine derivatives; it was applied by us to bromine compounds

$$CH_3CH=CH_2 + HBr \xrightarrow[C_6H_5NO_2]{AlCl_3} CH_3CHBrCH_3.$$

It was established that in the case of the addition of hydrogen bromide, too, it is possible to use aluminum chloride as a catalyst; in this case, a mixture of halogen derivatives is not formed, since the aluminum bromide, which is formed by the equilibrium reaction

$$AlCl_3 + 3HBr \rightleftharpoons AlBr_3 + 3HCl,$$

immediately reacts with the chlorine derivative which is formed, replacing the halogen atom:

$$3RCHClCH_3 + AlBr_3 \rightarrow 3RCHBrCH_3 + AlCl_3.$$

It should be pointed out that the method proposed by us almost completely excludes the possibility of the polymerization of the olefin, since a nitrobenzene solution of aluminum chloride at room temperature does not show polymerizing action on such substances as propylene and n-butylene.

There are analogous advantages in the method of the addition of hydrogen halides to olefins, based on the use of an ether solution of aluminum chloride [4]; it is desirable to use this method for obtaining of compounds with high boiling points, which are difficult to separate from nitrobenzene by distillation.

The following compounds were obtained by the method described above: ethylidene chloride (56-58°, d_4^{20} 1.1750, n_D^{20} 1.4166) from vinyl chloride, with a yield of 85%; methyl chloroform (73-75°, d_4^{20} 1.3162, n_D^{20} 1.4194) from vinylidene chloride, with a yield of 75%; isopropyl chloride (36-37°, d_4^{20} 0.8610, n_D^{20} 1.3782) from propylene, with a yield of 60%; isopropyl bromide (58-60°, d_4^{20} 1.3145, n_D^{20} 1.4250) from propylene and HBr, with a yield of 70%; 1,2-dichloropropane (96-98°, d_4^{20} 1.1561, n_D^{20} 1.4395) from allyl chloride, with a yield of 65%; 1,2-dibromopropane (139-142°, d_4^{20} 1.9310) from allyl bromide and, HBr with a yield of 60%; sec-butyl chloride (67-69°, d_4^{20} 0.8721, n_D^{20} 1.3966) from n-butylene, with a yield of 70%.

In all cases the addition of the hydrogen halide was carried out in accordance with Markovnikov's rule.

EXPERIMENTAL

The method of carrying out the syntheses is given below; the preparation of ethylidene chloride and methyl chloroform are given as examples.

The preparation of ethylidene chloride. The apparatus for the preparation of ethylidene chloride consists of a flask, or better still, of a column, with a bubbler and a reflux condenser. 50 ml of a 10% solution of aluminum chloride in nitrobenzene is poured into the flask; during the reaction it is cooled with a water bath. Vinyl chloride and hydrogen chloride are passed separately through rheometers, mixed in a T-pipe, passed through a drying column containing roasted calcium chloride, and through a safety flask, and enter the reaction vessel through the bubbler. The speed of the gas is regulated by the rheometer in such a way that a 5-10% excess of hydrogen chloride is supplied. In order to observe the course of the reaction, it is desirable to place (after a safety flask) a Drexel bottle at the outlet of the reflux condenser. The speed of the vinyl chloride is regulated in this case in such a way that only individual rare bubbles of the gas pass through this bottle. After the end of the reaction process, the liquid is decomposed with dilute hydrochloric acid in a separatory funnel and washed with water. Further separation of the product may be carried out in two ways: 1) by steam distillation, separation from the water, drying with calcium chloride, and final distillation; 2) drying with calcium chloride, distillation of the product until the temperature of the vapor is 120°, and final distillation.

The final result in both cases is the gathering of a fraction boiling at 56-58°. From one mole of vinyl chloride, 80-85 g of ethylidene chloride (up to 85%) was obtained.

Isopropyl chloride and bromide, and sec-butyl chloride were obtained by the same method.

The preparation of methyl chloroform. The apparatus for the preparation of methyl chloroform consists of a flask with a bubbler, a reflux condenser, and a dropping funnel. The flask is placed in a cold water bath, and is charged with 50 ml of a 10% solution of aluminum chloride in nitrobenzene. The air is forced out of the apparatus with dry hydrogen chloride, and 67 g of vinylidene chloride, which has been previously dried, is added by drops from the funnel, the hydrogen chloride being passed through at the same time. The rate of the gas flow was regulated in such a way that the passage of the gas from the apparatus was insignificant.

The reaction was completed when, after all the vinylidene chloride had been added, no more hydrogen chloride was absorbed. The separation of the product was carried out as in the preceding example. A final fraction, boiling at 73-75° was collected. The yield was 100 g (75%).

SUMMARY

1. It has been found that nitrobenzene complexes of aluminum chloride are not capable of decomposing halogen derivatives into olefins and hydrogen halides.

2. This made possible the proposing of a new method for the obtaining of certain halogen derivatives by the addition of hydrogen halides to olefins or chloro.olefins, under the catalytic action of a solution of aluminum chloride in nitrobenzene.

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CATALYTIC TRANSFORMATIONS OF THE HALOGEN DERIVATIVES OF THE AROMATIC SERIES

III. THE MECHANISM OF THE ISOMERIZATION OF THE MONO-HALOGEN DERIVATIVES OF NAPHTHALENE

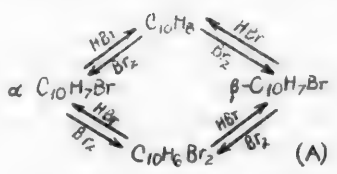
N. N. Vorozhtsov and N. M. Przhiyalgovskaya

It was shown earlier by one of us and A. M. Beskin [1], that the isomerization of monochloronaphthalenes by aluminum oxide in the presence of hydrogen chloride is a reversible process, which takes place without the noticeable formation of any by-products:

$$\alpha\text{-}C_{10}H_7Cl \underset{400^\circ}{\overset{Al_2O_3,\ HCl}{\rightleftharpoons}} \beta\text{-}C_{10}H_7Cl.$$

Unlike the monochloronaphthalenes, the reversible isomerization of monobromonaphthalenes in the presence of the halogen salts of iron and hydrogen bromide, is always accompanied by the formation of considerable quantities of naphthalene and dibromonaphthalenes. In the opinion of some Dutch investigators [2], the isomerization of monobromonaphthalenes is caused by the reversibility of the process of bromination. The equilibrium between the isomers is established indirectly through the formation of napthhalene and bromine according to scheme A.

It was established by us that catalytic isomerization of monobromonaphthalenes by aluminum oxide in the presence of hydrogen bromide, is also accompanied by the formation of naphthalene and dibromonaphthalenes. However, the data obtained by us on the study of the isomerization of monobromonaphthalenes shows that the intermolecular mechanism shown above cannot explain all the peculiarities of this process.



(A)

Thus, on the carrying out of the isomerization of monobromonaphthalenes in the presence of benzene, one of the products of the reaction is bromobenzene. If we assume only the intermolecular mechanism of the transformation of one isomer into the other, then the addition of benzene should lessen the degree of isomerization, since part of the bromine is combined with benzene in the form of bromobenzene.

Our experiments showed that on the increasing of the molecular ratio of benzene to 1-bromonaphthalene, the quantity of the naphthalene in the reaction product rises greatly (up to 59% with 6.3 moles of benzene to 1 mole of bromonaphthalene), but that the content of the 2-isomer in the fraction of nonobromonaphthalenes was decreased practically not at all, and constituted 56% of the total.

The addition of benzene in the isomerization of chloronaphthalene in the presence of hydrogen chloride does not influence the course of the process in any way, since the reaction of the chlorination of naphthalene at 350° is practically not reversible.

Experiments on the isomerization of 1-bromonaphthalene by aluminum oxide in a stream of hydrogen fluoride also indicate that there is no dependence between the degree of isomerization and the quantity of naphthalene formed. At 250°, the isomerization of 1-bromonaphthalene reached 54.5%, practically no naphthalene being formed (3.3% naphthalene in all). Hydrogen bromide was discovered in the gases escaping from the reaction tube. Investigation of the reaction product showed that in this case there was no exchange reaction between bromine and fluorine [3], and therefore, the formation of hydrogen bromide can be explained only by the partial pyrolysis of bromonaphthalene. The presence in the system of a small quantity of hydrogen bromide also caused, evidently, a correspondingly small disproportionation.

The raising of the temperature to 550° in the isomerization of 1-chloronaphthalene in the presence of hydrogen chloride, led to the formation of naphthalene in this case too (29.4%). The content of the 2-isomer in the fraction of monochloronaphthalenes was 52.5%.

The formation of the naphthalene was evidently caused by the fact that at high temperatures, with a catalyst, the reaction of the chlorination of naphthalene becomes reversible:

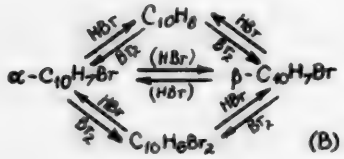
$$C_{10}H_7Cl + HCl \underset{550°}{\overset{Al_2O_3}{\rightleftharpoons}} C_{10}H_8 + Cl_2.$$

The absence of dichloronaphthalenes in the reaction product can be explained by their decomposition, as a consequence of the high temperature of the experiment (550°). It is known that some dichloronaphthalenes are decomposed even at their boiling points (~ 300°).

All of the facts given above can be explained by the fact that the isomerization of both chloro- and bromonaphthalenes, in the presence of halogen halides and aluminum oxide, in the gaseous phase, takes place according to an intramolecular mechanism. Along with isomerization in the strict sense, intermolecular transformation of one isomer into another is also possible, with the intermediate formation of the naphthalene and the halide, as a consequence of the reversible character of the halogenation reaction. This transformation takes place only on the appearance of the reducing properties of the hydrogen halide, in the presence of which the isomerization is carried out.

In connection with this, the scheme proposed by the Dutch writers does not fully reflect the isomeric transformations of the bromonaphthalenes in the presence of hydrogen bromide. A new scheme (B) was proposed by us for this case; it includes both the intramolecular and the intermolecular transformations of the monobromonaphthalenes.

The data obtained by Brezhneva and Roginsky [4], on the investigation of the isomerization of monobromonaphthalenes in the presence of $AlBr_3$ containing a radioactive bromine atom, also indicates the intramolecular mechanism of the reaction.



(B)

(Catalyst: $FeCl_3$, Al_2O_3).

The proposed dual mechanism of the isomerization of chloro- and bromonaphthalenes is not unique. The isomerization of naphthalene sulfonic acid [5, 6] evidently takes place in an analogous manner.

In connection with the above, it is necessary to point out that Favorsky [7], on the basis of an enormous amount of experimental data, came to the conclusion that isomeric transformations in the aliphatic series are intramolecular reactions.

Our investigations show, in our opinion, that the point of view of Favorsky on isomeric transformations is also applicable to the isomerization of naphthalene derivatives. Intermolecular transformations are linked only with the subsidiary processes which take place.

EXPERIMENTAL•

The interaction of 1-chloro- or 1-bromonaphthalenes with hydrogen chloride or hydrogen bromide, in the presence of benzene.

The experiments were conducted at 350° over aluminum oxide. The speed of input of the solution of the naphthalene halide into the benzene was 5-6 ml/hour, that of the hydrogen halide was 55 ml/minute. The results of the experiments are given in Table 1. For comparison, the quantity of naphthalene formed in the absence of benzene is also given here.

Upon the distillation of the products of catalysis of reactions I, II and III, carried out in the presence of benzene, fractions with a boiling point of 152-154° and n_D^{20} 1.5594 were isolated in all three cases. The data given in the literature for bromobenzene are: boiling point 156.2° and n_D^{20} 1.5604 [8]. For identification the product was nitrated with nitric acid to the dinitro derivative. After recrystallization from dilute ethanol, yellow crystals were obtained in the form of small needles with a melting point of 72-73°. The literature data for 2,4-dinitrobromobenzene gives a melting point of 73°. After the determination of the melting point, a mixture test was carried out with known 2,4-dinitrobromobenzene; no depression of the melting point was observed. Thus, one of the products of reactions I, II and III is bromobenzene.

• The apparatus and the method of work have been described in the previous communication [3].

TABLE 1

Reaction	I α-$C_{10}H_7Br$ + + HBr	II α-$C_{10}H_7Br$ + + HCl	III α-$C_{10}H_7Cl$ + + HBr	IV α-$C_{10}H_7Cl$ + + HCl
Quantity of naphthalene in the absence of benzene (in mole %)	20.8	22.4	22.1	0
Quantity of naphthalene in the presence of 2.5 moles of benzene per 1 mole of the naphthalene halide	39.9	26.4	38.8	0

TABLE 2

Number of moles of benzene per 1 mole of 1-bromonaphthalene	Quantity of naphthalene formed (in mole %)	Fraction of monobromonapthalenes	
		Solidification point	Content of the 2-isomer (in weight %)
0	20.8	19.1°	56.2
2.5	39.9	18.9	56.0
4.3	52.2	18.4	55.5
6.3	59.0	18.7	55.7

The influence of the ratio of benzene to 1-bromonaphthalene on the reaction of isomerization of 1-bromonaphthalene, in the presence of hydrogen bromide. The experiments were carried out at a temperature of 350° over aluminum oxide. Each experiment was continued for 3 hours. The speed of input of the bromonapthalene solution in benzene was 5-6 ml/hour, the speed of HBr – 55 ml/minute. The results of the experiments are given in Table 2.

The interaction of 1-bromonaphthalene with hydrogen fluoride. The experiment was carried out at 250°. 3.53 g (0.170 mole) of 1-bromonaphthalene and 30 g (1.5 mole) of hydrogen fluoride were passed through aluminum oxide for three hours. The product of catalysis was washed, and subjected to fractionation (25.68 g) at atmospheric pressure. The following fractions were collected: the first with a b. p. of 215-220°, 0.46 g, freezing point, 49.5°; second b. p. 220-275°, 0.54 g, freezing point 34.2°; the third, b. p. 275-282°, 18.10 g, freezing point 17.1°; the fourth, b. p. 282-285°, 2.6 g; the residue 2.9 g.

0.004 mole of hydrogen bromide was found in the gases escaping from the reaction tube.

About 70 mg of the substances of the first and second fractions was melted with metallic potassium in a steel bomb. The qualitative test of the melt with zirconium chloride for fluorine [9], gave negative results. This indicates that the first and second fractions are, as is usual on the isomerization of 1-bromonaphthalene, mixtures of naphthalene and monobromonaphthalenes. The quantity of naphthalene formed is 0.73 g (0.0058 mole), or 3.34% of the number of moles of 1-bromonaphthalene originally passed over the aluminum oxide.

According to the freezing point, the third fraction contains 54% 2-bromonaphthalene.

Isomerization of 1-chloronaphthalene over aluminum silicate in a stream of hydrogen chloride at 550°. The experiment was carried out at 550° and the speed of the hydrogen chloride was 60 ml/minute. 18 g (0.11 mole) of 1-chloronaphthalene was passed through for three hours. The product of catalysis (14.23 g) was a solid substance, lemon-yellow in color. On distillation 12.8 g of the following fractions was collected; the first had a b. p. of 217-225°, 2.4 g, freezing point 76.3°; the second has a b. p. of 225-255°, 3.45 g, freezing point 42.1°; the third, b. p. 255-260°, 5.41 g, freezing point 20.1°; there was 0.9 g of residue.

The first fraction was naphthalene. The quantity of naphthalene formed was 4.16 g (0.0325 mole) or 29.4% of the number of moles of 1-chloronaphthalene originally passed through. The third fraction contained 52.5% 2-chloronaphthalene.

In the course of the experiment, the uncondensed gases, escaping from the receptacle for the products of catalysis, were collected with a 4% aqueous solution of potassium iodide in two successive, connected bottles. In the first bottle the solution became dark red. It was established by iodometric means that in the course of the experiment, 0.00204 mole of chlorine was given off.

SUMMARY

1. The isomerization of chloro- and bromonapthalenes (in the gaseous phase) over aluminum oxide, in the presence of hydrogen halides (HF, HCl, HBr) has been studied.

2. It has been shown that the isomerization of both the chloro- and bromonapthalenes takes place by an intramolecular mechanism. Along with the normal isomerization, under these given conditions it is also possible to have the intermolecular transformation of one isomer into another, with the intermediate formation of naphthalene and a halide, as a consequence of the reversible character of the reaction of halogenation.

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INVESTIGATIONS IN THE FIELD OF MOLECULAR CHROMATOGRAPHY

1. SEPARATION OF MIXTURES OF NITROPHENOLS

K. A. Ogloblin and G. V. Markina

There is very little literature data on the chromatographic separation of mixtures of nitrophenols.

On the separation of mixtures of the three isomeric mononitrophenols from benzene over calcium carbonate (they were passed over twice), Karrer and Nielsen found, that the adsorbability of the compounds falls in the series para-nitrophenol, meta-nitrophenol, and ortho-nitrophenol in that order [1]. The order of the adsorption, on polar adsorbents, of nitrophenols and other compounds, was set down in a short communication by Arnold [2]; he reported that this order depended on the size and number of the separate dipoles in the molecule. On the carrying out of chromatographic investigations of many nitro derivatives of the aromatic series from mixtures of petroleum ether with benzene and acetone, on silica gel mixed with celite, Ovenston established the place of some nitrophenol compounds in the adsorption series of the various nitro derivatives [4]. The literature data on the quantitative chromatographic separation of mixtures of nitrophenols is limited to the work by Norvall and Kenyon on the separation of two binary mixtures (para-nitrophenol with 2,6-dinitro-o-cresol and with 2,4-dinitro-α-naphthol) from ether over aluminum oxide (3).

From the available literature data, it is difficult to get an idea of the connection between the structure and physical-chemical properties of the nitrophenols, and their behavior under the conditions of chromatographic separation. But the establishment of such a dependence is a necessary condition for the rational utilization of the chromatographic method.

The order of adsorption of mixtures of substances depends on many factors, including the structure and properties of the compounds, the chemical nature and properties of the adsorbent, and the properties of the solvent used. In spite of this, it is possible to assume that under certain definite conditions the predominate influence of some factors will be observed, and that with a change in conditions, other factors will exert the main influence. An example of this is the known phenomenon of the change in the order of the adsorption of mixtures of substances, on the very same adsorbent, with a change in solvents [5]. Starting from this fact, it is impossible to consider correct that point of view which considers one of the factors, regardless of the concrete conditions, responsible for the order of the adsorption of mixtures; therefore, it is impossible to agree with Arnold's opinion [2], which recognizes the importance of the dipole and denies the importance of the acidity and basicity of the compounds, without taking into account the concrete conditions of the experiment.

On undertaking the investigation of the series of mixtures, we set as our goal the finding of the optimal conditions for their separation, and the discovery of those physico-chemical properties of the compounds, which, in the given concrete conditions, determined the order of their adsorption.

In the present communication are contained the results of work on the chromatographic separation of artificial mixtures of nitrophenols from non-polar solvents, or from solvents with a small degree of polarity, over aqueous aluminum oxide.

The following artificial mixtures of nitrophenols were taken for separation: 1) ortho-nitrophenol, meta-nitrophenol, para-nitrophenol, and 2,4-dinitrophenol in benzene, the developer – benzene; and 2) 2,4-dinitrophenol, 2,5-dinitrophenol, and 2,6-dinitrophenol in benzene, the developer – benzene and its mixture with ether.

For the separation, a commercial preparation of aluminum oxide which had been previously moistened, was used. Commercial aluminum oxide has an exceptionally great adsorption capacity for nitrophenol, as a consequence of which the chromatogram for such an oxide is a series of stably fixed, narrow adjoining zones, which makes the separation much more difficult. The most satisfactory results were obtained for aluminum which contained 14.3-15.5% water (desiccation at 110-115°) i.e. on the adsorbent with a greater moisture content than any of those prepared by Brochmann [6]. The chromatographic analysis was carried out under a small excess of pressure. Observation of the

course of the separation was by visual means, since all the nitrophenols were colored. On washing with a solvent, part of the nitrophenols were washed out in the filtrate and those remaining in the column were extracted with a mixture of benzene and hydrochloric acid (see the experimental section of this paper).

Under the conditions of the experiment, both mixtures were fully divided into their component parts, the first mixture, after one passage through the column.

The results obtained in our experiments make it possible to arrange the nitrophenols in the following adsorption series (in order of increasing adsorbability):

For mixtures of four nitrophenols –

$$o\text{-}C_6H_4(OH)NO_2 < m\text{-}C_6H_4(OH)NO_2 < p\text{-}C_6H_4(OH)NO_2 < 2,4\text{-}C_6H_4(OH)(NO_2)_2;$$

For mixtures of three dinitrophenols –

$$2,5\text{-}C_6H_3OH(NO_2)_2 < 2,4\text{-}C_6H_3OH(NO_2)_2 < 2,6\text{-}C_6H_3OH(NO_2)_2.$$

In the evaluation of the results obtained, we took into account a number of factors. First of all, the experiment showed that nitrophenols are exceptionally stably held by aluminum oxide, and that it is very difficult to wash them out of the column with non-polar (benzene) or slightly polar (ethyl ether) solvents. An exception to this rule, to a certain extent, is ortho-nitrophenol; this difference is evidently linked with the presence in this compound of a strong, intramolecular hydrogen bond, which brings about its increased solubility. At the same time, the dinitrophenols are so firmly held by the aluminum oxide that they are not washed out fully even with ethyl alcohol. In addition, our attention is attracted by the considerably brighter color of the nitrophenols in the column compared to their color in the free state. We should also keep in mind the acid character of the nitrophenols and the possibility of the manifestation of the basic properties of aqueous aluminum oxide.

All this compels us to assume that under our conditions of the separation of the mixtures, the chemical interaction of the nitrophenols with aluminum oxide exerts a considerable influence on the order of adsorption. In accordance with this, the order of the adsorption of nitrophenols over aqueous aluminum oxide should be determined, mainly, by the degree of their acidity, i.e., the adsorbability of the nitrophenols should change parallel with their dissociation constants. In Table 1 are given the values of the dissociation constants and the order of adsorption of the nitrophenols, found by us on the separation of mixtures of four nitrophenols.

TABLE 1

Name of the compound	Distribution in the column (from the bottom up)	Dissociation constants [7]
Ortho-nitrophenol	I	$7.5 \cdot 10^{-8}$ (25°)
Meta-nitrophenol	II	$1.0 \cdot 10^{-8}$ (25°)
Para-nitrophenol	III	$9.6 \cdot 10^{-8}$ (25°)
2,4-Dinitrophenol	IV	$1.0 \cdot 10^{-4}$ (25°)

TABLE 2

Name of the compound	Distribution in the column (from the bottom up)	Dissociation constants [7]
2,5-Dinitrophenol	I	$7.0 \cdot 10^{-6}$ (25°)
2,4-Dinitrophenol	II	$1.0 \cdot 10^{-4}$ (25°)
2,6-Dinitrophenol	III	$2.0 \cdot 10^{-4}$ (25°)

As is evident from the data of Table 1, the order of distribution of the nitrophenols in the column, on the separation of mixtures of them from non-polar solvents, over aqueous aluminum oxide, is in correspondence with the order of the changes in the values of the dissociation constants. The anomalous position of ortho-nitrophenol shows precisely that the degree of acidity of the nitrophenols is only one of the factors, which acts along with the other factors such as, the solubility, polarity, tendency toward the formation of hydrogen bonds with hydrated surfaces of the absorbent, etc.

On the chromatographic analysis of the mixture of the three dinitrophenols, the lowest in the column was 2,5-dinitrophenol and the highest was 2,6-dinitrophenol, i.e., the order of adsorption in this case corresponded with the order of the change in the dissociation constants (Table 2).

The correspondence in the values of the dissociation constants of the nitrophenols is reflected on the chromatograms obtained in our experiments in such a way that between the zones of the compounds with strongly differing constants, narrow "empty" zones appeared after development (para-nitrophenol and 2,4-dinitrophenol); at the same time, nitrophenols with dissociation constant values that were close to each other formed adjoining zones (para-nitrophenol and meta-nitrophenol, 2,4- and 2,6-dinitrophenol). In the latter case, quicker separation was possible through the use of mixtures of benzene and ether for washing.

In conclusion, it should be pointed out that aqueous solutions of aluminum oxide can be used for the separation of mixtures of nitrophenols of any composition, since there are considerable differences in the dissociation constants of all nitrophenols. It is possible to suppose that, in general, on chromatographic analysis over aqueous aluminum oxide from non-polar or slightly polar solvents (benzene, ether), of mixtures of organic acids of one class, such as nitrophenols, nitraminic acids, nitrobenzoic acids, etc., the order of their adsorption will be determined, to a considerable extent, by their degree of acidity.

EXPERIMENTAL

The apparatus for the chromatographic separation consisted of a glass tube with an outlet pipe soldered in the upper part and a slightly drawn out lower end. The top of the tube was connected to a dropping funnel with a polished section or with a rubber stopper. A thick wad of glass wool was placed in the narrow lower part of the tube; a layer of the adsorbent was placed on the glass wool. The equal distribution of the adsorbent was achieved by tapping on the walls of the tube with a glass rod which was covered with a piece of rubber tubing, until the level of the adsorbent ceased to fall. A small piece of filter paper was placed over the layer of the adsorbent. The outlet pipes of the tube and the dropping funnel were connected through a T-pipe to a U-shaped mercury manometer and a three-liter buffer bottle, connected by a hose to a water faucet. The pressure in the buffer bottle and in the apparatus was built up and maintained at the desired level by the periodic opening of the water faucet.

"Aluminum oxide for chromatography", series no. 15, produced by the Stalin factory, was used in the experiments. The aluminum oxide had been previously moistened to the necessary percentage of moisture by the addition of the calculated quantity of distilled water. The mixture was shaken in a closed flask for 2 hours, after which the adsorbent was kept in the closed flask for 24 hours. Moistening the adsorbent in this way guaranteed the homogeneity of the adsorbent; this was evident from the chromatograms and from the analytical data on the percentage of moisture. The determination of the amount of moisture was carried out by means of the drying of a weighed portion of aluminum oxide until constant weight at 110-115°. In addition, the total percentage of water was determined by the roasting of the adsorbent at 550-600° for half an hour. As solvents for the preparation of the original mixtures, development, and the washing of substances out of the column, benzene (ordinary purification with sulfuric acid and distillation in a distillation column) and anhydrous ethyl ether were used.

On the washing of the column, part of the nitrophenols went out with the filtrate, and the most stably adsorbed nitrophenols were extracted from the adsorbent with hydrochloric acid. The differently colored zones of the adsorbent, which were extracted from the column, were shaken in a bottle with a ground glass stopper, with a mixture of benzene and dilute hydrochloric acid (acid with a specific gravity of 1.19 was diluted with an equal volume of water). After 3 or 4 such workings of the adsorbent, practically all of the adsorbed substance went over into the benzene solution; the nitrophenol was separated from the benzene by the vacuum distillation of the solvent. The obtained crystals were dried in a vacuum-desiccator over aluminum oxide, after which they were weighed, and their melting point was determined. Difference in the weight of the nitrophenol separated in this way to the quantity of it in the original mixture was considered the yield of the product. Although the substances in the column were usually fully separated, their yield, with rare exceptions, was always below 100%; this was because of losses due to the discarding of the intermediate zones (in the case of adjoining zones) and those that occurred during the extraction of the nitrophenols from the adsorbent.

Separation of the mixture of ortho-nitrophenol, meta-nitrophenol, para-nitrophenol, and 2,4-dinitrophenol over aluminum oxide. 25 ml of a benzene solution containing 0.10 g each of ortho-, meta-, and para-nitrophenol, and 2,4-dinitrophenol was chromatographically analyzed in a column containing aluminum oxide (the column was 452 by 13.5 mm). The loss in weight of the adsorbent on roasting to 550-600° was 20.65-20.66%; the loss on drying at 110-115° was 14.25-14.30%. 200 ml of benzene was used as the developer; the excess pressure was 100 mm; the temperature was 17°. As a result of washing with benzene the following fractions of the filtrate were obtained (according to the rate of flow): the first was a light yellow, from the wide (215 mm) yellow zone; light yellow crystals in the form of needles were separated; weight 0.06 g (60%)* m. p. 46.5-47°; in a mixture test with ortho-nitrophenol (m. p. 44.7-45.5°) the mixture had m.p. 45-45.5°; the second fraction was light yellow from the wide light yellow zone (240 mm); the weight of the light yellow crystals, 0.07 g (70%), m. p. 97.4-97.7°; the mixed sample with meta-nitrophenol (m. p. 97.2-97.7°) melted at 97.6-97.8°.

The rest of the components of the mixture remained in the column in the form of a series of colored zones (from bottom to top); greenish yellow, width 120 mm (third fraction); bright yellow, 53 mm, (fourth fraction).

* The relatively low yield of ortho-nitrophenol is explained by losses on drying [8].

Between the third and fourth fractions there was a white space about 2-3 mm wide. The colored zones of the adsorbent were extracted from the column with a spatula, and the parts on the boundary lines were discarded. After the working of each of the zones with a mixture of benzene and hydrochloric acid, fractions of the following crystals were obtained: the third – light yellow, long plates, weight 0.10 g (100%), m. p. 113-114°, the mixed sample with para-nitrophenol (m. p. 113.5-114.5°) melted at 113.5-114.6°; the fourth fraction – light yellow needles, weight 0.09 g (90%), m. p. 114-114.5°, the mixed sample with 2,4-dinitrophenol (m. p. 113.5-114°) melted at 113.4-114.0°.

The separation of the mixture of 2,4-, 2,5-, and 2,6-dinitrophenol over aluminum oxide. 10 ml of a benzene solution containing 0.10 g each of 2,4-, 2,5-, and 2,6-dinitrophenol was chromatographically analyzed over a column containing aluminum oxide; the size of the column was 178 by 14 mm. The adsorbent was humidified aluminum oxide, the loss of weight on roasting (550-600°) was 21.97-22.00%, the loss on drying (110-115°) was 15.47-15.49%; 40 ml of benzene was used as the developer, then a mixture of benzene with ether was used (100:1) 10 ml, (100:5) 19 ml, (1:1) 60 ml; ether 120 ml. The excess pressure was 20 mm, the temperature was 18°. After washing with the solvents, the following fractions were obtained.

1) A yellow filtrate from the orange zone (80 mm). Reddish yellow crystals, weight 0.08 g (80%), m. p. 108.5-109.5°. After repeated chromatographic analysis over the same oxide, a narrow, bright red zone which was not investigated was separated; 20 ml of the solution was used, 32 ml of benzene was used as the developer, the column was 104 by 10 mm, the pressure was 40 mm, and the temperature was 19°. From the main orange zone 0.07 g (70%) of yellow crystals was isolated; m. p. 108.3-108.7°, mixed sample with 2,5-dinitrophenol (m. p. 104-106°) melted at 105.2-106°.

2) The greenish yellow zone of the column (25 mm). After extraction from the column and the working of the adsorbent with a mixture of benzene and hydrochloric acid, 0.06 g (60%) of greenish yellow plates and needles was isolated; m. p. 115-115.7°, the mixed sample with 2,4-dinitrophenol (m. p. 113.5-114°) melted at 115-115.5°.

3) 0.04 g of yellow crystals was extracted with benzene and hydrochloric acid from each of the adjoining light orange (15 mm) and bright yellow (31 mm) zones of the adsorbent; m. p. 57-58° and 54-55°, mixed samples with 2,6-dinitrophenol melted between 57 and 60°. The substance was purified chromatographically over the same oxide, from benzene (10 ml of the solution, developer 110 ml of benzene, size of column 123 by 10 mm, pressure 40 mm, and temperature 19°). The main bright orange zone of the adsorbent (22 mm) was separated from the two narrow strips corresponding to the border regions (the lower – yellow, 1.5 mm, the upper – muddy orange, 0.5 mm). 0.07 g (70%) of yellow crystals was extracted from the bright orange zone with benzene and hydrochloric acid; m. p. 60-60.5°, the mixed sample with 2,6-dinitrophenol (m. p. 61-61.5°) melted at 60.3-61.5°.

SUMMARY

1. Chromatographic separations have been carried out on mixtures of ortho-nitrophenol, meta-nitrophenol, and para-nitrophenol and 2,4-dinitrophenol, and on mixtures of 2,4-, 2,5-, and 2,6-dinitrophenols; the separations were conducted from benzene and ether, over aqueous aluminum oxide.

2. It has been established that the order of adsorption of the indicated nitrophenols from benzene and ether over aqueous aluminum oxide corresponds to the order of their dissociation constants.

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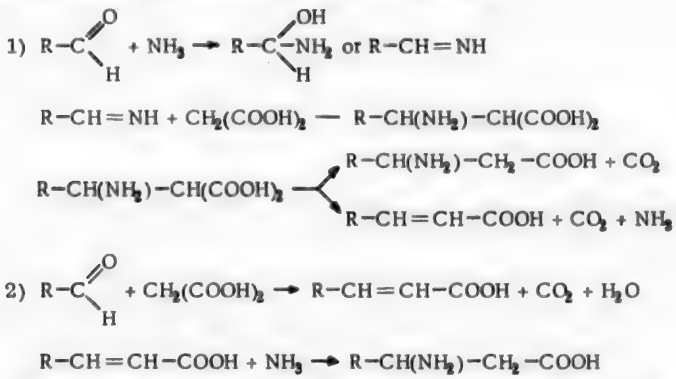
THE SYNTHESIS OF α-ALKYL-β-PHENYL-β, N-ALKYLAMINOPROPIONIC ACIDS AND SOME OF THEIR DERIVATIVES

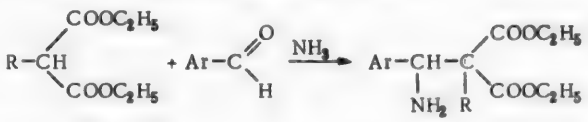
V. M. Rodionov* and K. P. Preobrazhenskaya

The purpose of the present work was the obtaining of C-alkylated and N-alkylated β-aminocarboxylic acids, and the comparison of their properties and transformations with β-amino acids which have a primary amine group. This work was undertaken in order to clarify the mechanism of the reaction of the formation of β-amino acids.

In the works of V. M. Rodionov and co-workers, two schemes of the formation of β-amino acids have been proposed; they may be represented in the following way:



The second scheme is less probable, since it has been shown in the work of Rodionov and Postovskaja [1] that the esters of mono-substituted malonic acid, under the conditions of the Rodionov reaction, give the esters of α-alkyl-β-aryl-β-aminoethane-α,α-dicarboxylic acids:

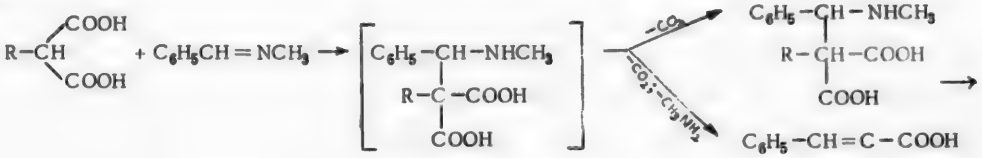


where R equals alkyl

and, as is evident, in this case α, β-unsaturated acids or their esters cannot be formed.

In favor of the first scheme there are many facts, which have been pointed out both in the works of the school of V. M. Rodionov [2, 3], and by some Soviet [4] and foreign [5] authors.

In order to confirm the first scheme of the mechanism of the reaction of the formation of β-amino acids and to prove that various substituted malonic acids are capable of being added to aldimines, we synthesized several α-alkyl-β-phenyl-β, N-alkylaminopropionic acids. This synthesis was accomplished by means of the interaction of alkylmalonic acids with benzalmethylamine, the readily accessible first representative of the aliphatic-aromatic aldimines:



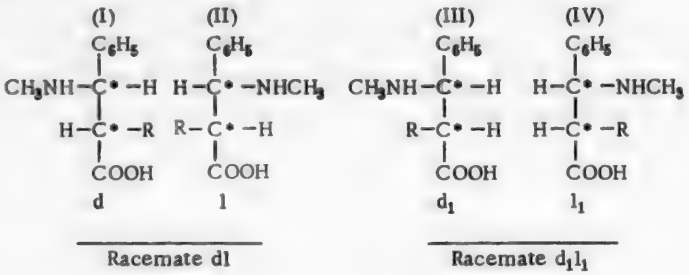
where R = alk.

*Deceased.

The addition of the alkylmalonic acids (ethyl-, butyl-, and benzyl-) was carried out with complete success, which served as a new confirmation of the first scheme.

On the carrying out of these reactions, it was also established that, along with the formation of the alkylated β-amino acids, the corresponding unsaturated acids are always formed.

On the synthesis of α-alkyl-β-phenyl-β, N-alkylaminopropionic acids by the Rodionov reaction, acids with two asymmetrical carbon atoms were obtained. Consequently, one may expect four optically active forms, and, therefore, two racemates.



where R equals an alkyl group.

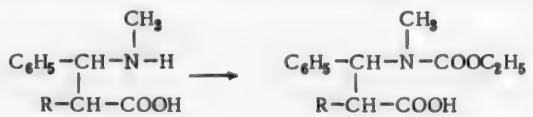
Thus, we must have here two different pairs of optical antipodes, and each pair, on being mixed in equal quantities, should give an inactive substance. The stereoisomers of configurations (I) and (III) and also (II) and (IV), while they are not antipodes, turn out to be diastereoisomers.

And, actually, it was established by us that on the synthesis of α-alkyl-β-phenyl-β, N-methylaminopropionic acids, two acids (two diastereoisomers) are always obtained; this also confirms the first scheme suggested above.

The separation of the two diastereoisomeric forms was accomplished by means of fractional crystallization from alcohol.

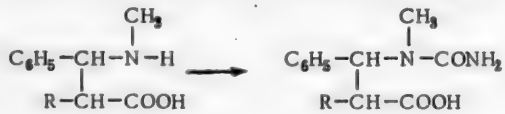
Further reactions for α-ethyl-β-phenyl-β, N-methylaminopropionic, α-N-butyl-β-phenyl-β-N-methylaminopropionic, and α-benzyl-β-benzyl-β-phenyl-α-Nmethylaminopropionic acids have been carried out so far with only one of the diastereoisomeric forms which have been isolated. In order to determine the characteristics of the α-alkyl-β-phenyl-β,N-alkylaminopropionic acids which were synthesized, some of their derivatives were prepared.

1. The carboethoxy derivatives of α-alkyl-β-phenyl-β,N-alkylaminocarboxylic acids were prepared in the usual way by the action of the chlorocarbonic ester on the alkylated β-amino acid in an alkaline medium [6].



Where R equals H, alkyl group.

2. Some alkylated β-ureido-acids were also prepared, since, as is known, they are very characteristic compounds for amino acids and are often used for the identification of the latter.



Where R equals H, alkyl group.

3. Alkylated β-ureido acid was successfully converted into alkylated dihydrouracil, water being split off in the process.

Where R equals H, alkyl group.

On the closing of β-phenyl-β, N-1-methylureidopropionic acid, 3-N-methyl-4-phenyldihydrouracil was definitely obtained; this was fully confirmed by the analysis of this substance. However, it melted at 164-165°, and not at 158-159.5°, as was indicated by Evans and Johnson [5] who were the first to obtain it.

The obtaining of carboethoxy derivatives, β-ureido acids, and dihydrouracils for alkylated β-aminocarboxylic acids, takes place analogously to the process involved for β-amino acids which contain a primary amino group.

It is necessary to point out that β-phenyl-β, N-benzylaminopropionic acid differs in a number of its chemical properties from the other alkylated β-amino acids.

Thus, attempts to prepare the carboethoxy derivative and the β-ureido acid for β-phenyl-β, N-benzylaminopropionic acid under the usual conditions used for the preparation of the derivatives of β-amino acids did not give positive results. This can evidently be explained by the fact that the accumulation of phenyl groups causes steric hindrance, similar to that which takes place in the case of the closing of ω-arylsubstituted ureido acids, which has been described in the literature [7].

EXPERIMENTAL

The preparation of α-ethyl-β-phenyl-β, N methylaminopropionic acid. A mixture of 7.09 g (0.059 mole) benzalmethylamine (b. p. 179-180°), 7.55 g (0.057 mole) of ethylmalonic acid (m. p. 111.5-112°), and 40 ml of anhydrous benzene were heated in a three-necked bottle, equipped with a reflux condenser, a mechanical stirrer, and a thermometer. The reaction was carried out gently at first at 55-60° for 2 hours (at this temperature the main reaction of decarboxylation takes place); then the reaction mixture was kept at 60-70° for two hours, and finally, the temperature was raised to 80-85° and maintained at that level for 6 hours. On the completion of the heating, the benzene was distilled off and anhydrous ether was added to the residue. The white precipitate was filtered off, washed several times with anhydrous ether, and dried. The yield – 5.35 g (45%). After two recrystallizations from alcohol 2.6 g of the substance (22%) was separated; its m. p. was 205-206°.

4.16 mg sub.: 10.58 mg CO_2; 3.19 mg H_2O. 7.51 mg sub.: 19.08 mg CO_2; 5.74 mg H_2O. 7.95 mg sub.: 0.453 ml N_2 (22°, 752 mm). 5.33 mg sub.: 0.318 ml N_2 (23°, 752 mm). Found %: C 69.37, 69.20; H 8.58, 8.54; N 6.68, 6.81. $C_{12}H_{17}O_2N$. Calculated %: C 69.56; H 8.21; N 6.77.

The obtained substance was α-ethyl-β-phenyl-β, N-methyl-aminopropionic acid.

After the solvent was driven off and anhydrous ether was added, a second isomer of α-ethyl-β-phenyl-β, N-methyl-aminopropionic acid was isolated from the mother liquor. After recrystallization from ligroine, 1.11 g of a substance with a melting point of 170° was obtained. A mixed sample of the two diastereoisomers of α-ethyl-β-phenyl-β, N-methylaminopropionic acid melted at 156-160°. 3.1 g (30%) of α-ethylcinnamic acid with a melting point of 104° was obtained from the ether solution, after the driving off of the solvent and recrystallization from water (the literature data gives 104-105° as the melting point).

The preparation of α-n-butyl-β-phenyl-β, N-methylaminopropionic acid. 8.6 g (0.054 mole) of n-butylmalonic acid (m. p. 101°) was introduced into a solution of 7.6 g (0.063 mole) of benzalmethylamine in 40 ml of dry benzene.

The reaction was carried out in a three-necked bottle, equipped with a mechanical stirrer and a reflux condenser. The reaction mixture was heated at 60-70° for 2 hours, then the temperature was gently raised to 80-85° and held there for 10 hours.

On the completion of the reaction, the benzene was distilled off; anhydrous ether (50 ml) was added to the residue, which consisted of a light yellow oil. The white precipitate which was isolated, was filtered, washed with anhydrous ether, and dried in a vacuum-desiccator. The yield was 5.74 g, the m. p. was 174-175° (without decomposition). From the filtrate was obtained an additional 2.18 g of the substance with a m. p. of 190-192°. The total yield was 7.92 g (62.8 %). The substances were separately recrystallized from alcohol.

From the 5.74 g, 3.43 g (27%) of substance with m. p. 183-184° was isolated on recrystallization. After two recrystallizations from alcohol the product had a melting point of 183-184° and recrystallized in the form of small needles.

From the 2.18 g (m. p. 190-192°), 1.8 g of a substance with a m. p. of 200-201° was obtained after recrystallization from alcohol. After two recrystallizations from alcohol, the yield was 1.16 g, the m. p. was 205°; the substance crystallized in the form of fine needles. A mixed sample of the two diastereoisomers (m. p. 183-184° and m. p. 205°) melted at 172-174°.

Analysis of the substance with m. p. 183-184°.

5.20 mg sub.: 13.57 mg CO_2; 4.43 mg H_2O. 5.65 mg sub.: 14.78 mg CO_2; 4.84 mg H_2O. 8.21 mg sub.: 0.412 ml N_2 (19.5°, 755 mm). 5.38 mg sub.: 0.268 ml N_2 (19.5°, 755 mm). Found %: C 71.21, 71.39; H 9.53, 9.58; N 5.81, 5.77. $C_{14}H_{21}O_2N$. Calculated %: C 71.49; H 8.93; N 5.95.

The synthesized substance is α-n-butyl-β-phenyl-β,N-methylaminopropionic acid; it is quite soluble in alcohol, benzene, acetone, and is slightly soluble in ether.

The corresponding unsaturated acid was isolated from an ether solution in the usual way. After recrystallization from dilute alcohol, 2.7 g (25%) of α-n-butylcinnamic acid was obtained. The melting point was 83° (according to the literature data the m. p. is 83-84°).

The obtaining of α-benzyl-β-phenyl-β,N-methylaminopropionic acid. a) A mixture of 14.6 g (0.075 mole) of benzylmalonic acid (m. p. 117-118°) and 10.1 g (0.084 mole) of benzalmethylamine in 60 ml of dry benzene was heated in a bottle with a reflux condenser over a water bath for two hours at 65-70°; even at this temperature the reaction of decarboxylation took place to an appreciable extent. The temperature was gradually raised and was held at 85° for 10 hours; thereupon, white crystals were formed on the walls of the bottle, and near the end of the period of heating the entire contents of the bottle consisted of a solid, white crystalline mass. The precipitate was filtered and was washed several times with anhydrous ether in order to separate it fully from the unsaturated acid; after this it was dried. The yield was 13.0 g (64.2%), the m. p. was 198-202°. After two recrystallizations from methyl alcohol 6.13 g (30.3%) with a m. p. of 218-219° was obtained.

5.04 g of the substance (about 25%) was isolated from the mother liquor after the driving off of the excess solvent and the addition of ether. After recrystallization from dilute alcohol, the yield was 4.13 g (20.4%) of a white crystalline powder with a melting point of 188-189°. The mixed sample of the two diastereoisomers (melting points 218-219° and 188-189°) melted at 180-183°.

Analysis of the substance with m. p. 218-219°.

3.91 mg sub.: 10.84 mg CO_2; 2.57 mg H_2O. 3.88 mg sub.: 10.77 mg CO_2; 2.53 mg H_2O. 4.38 mg sub.: 0.214 ml N_2 (21°, 738 mm). 4.65 mg sub.: 0.224 ml N_2 (22°, 738 mm). Found %: C 75.61, 75.70; H 7.35, 7.29; N 5.50, 5.41. $C_{17}H_{19}O_2N$. Calculated %: C 75.83; H 7.06; N 5.20.

The substance obtained is α-benzyl-β-phenyl-β,N-methylaminopropionic acid.

After the driving off of the solvent from the ether solution the precipitate began to crystallize.

On recrystallization from benzene, 3.73 g (20.8%) of α-benzylcinnamic acid was obtained; m. p. 156-157° (literature data: m. p. 158°).

b) A mixture of 6.28 g (0.06 mole) of benzaldehyde, 9.7 g (0.05 mole) of benzylmalonic acid, 5.05 g (0.075 mole) of methylamine hydrochloride, and 7.5 g of dehydrated potassium acetate in 25 ml of glacial acetic acid was placed in a flask equipped with a reflux condenser, and heated over a water bath; first, the mixture was heated at 70-80° for 1 hour, then, it was heated over a boiling water bath for 10 hours. Carbon dioxide was given off from the mixture, which was homogeneous at first, and a crystalline substance was precipitated out. The thick crystalline mass which was obtained on the cooling of the reaction mixture was extracted with dilute hydrochloric acid. The filtrate, which had been acidified with hydrochloric acid, was first concentrated over the water bath and then extracted two or three times with ether; the aqueous solution was neutralized with a concentrated solution of sodium acetate. In order to obtain full crystallization of the precipitate, it was allowed to stand for 24 hours; then, it was separated, washed with water, and dried. The yield was 7.56 g (56.4%), the m. p. was 189-192°. After two recrystallizations from methyl alcohol, 3.7 g of a substance with a m. p. of 218-219° was obtained in the form of fine, colorless needles. The substance was α-benzyl-β-phenyl-β,N-methylaminopropionic acid; a mixed sample, made with this substance obtained by other means, did not give a depression of the freezing point.

Preparation of β-phenyl-β,N-benzylaminopropionic acid. a) The following components were taken in equimolecular quantities: 10.30 g of benzylamine (b. p. 185-187°), 10.46 g of benzaldehyde, 10.09 g malonic acid, and 55 ml of dry benzene were heated in a flask equipped with a reflux condenser, over a water bath. The heating of the mixture was carried out gently at first, the temperature being kept at 60-70° for 3 hours; thereupon, bubbles of carbon dioxide were given off; a large quantity of a white, flaky precipitate fell to the bottom of the flask. 15 ml more of dry benzene was added to the precipitate and the mixture was heated for eight hours at 80-85°.

On the completion of the reaction, the benzene was distilled off and anhydrous ether (80 ml) was added to the residue; on cooling and stirring, a white, fine, crystalline precipitate was obtained, which was filtered, washed several times with anhydrous ether, and dried. The yield was 13.18 g (54%), the m. p. was 177-178°. After recrystallization from methyl alcohol 9.45 g (38.5%) of a substance with a m. p. of 183-184° was obtained.

Analysis of the substance with m. p. 183-184°.

4.12 mg sub.: 11.40 mg CO_2; 2.39 mg H_2O. 4.67 mg sub.: 12.94 mg CO_2; 2.81 mg H_2O. 6.01 mg sub.: 0.270 ml N_2 (19.5°, 755 mm). 7.48 mg sub.: 0.345 ml N_2 (19.5°, 755 mm). Found %: C 75.50, 75.61; H 6.49, 6.73; N 5.21, 5.35. $C_{16}H_{17}O_2N$. Calculated %: C 75.37; H 6.66; N 5.49.

The synthesized substance is β-phenyl-β,N-benzylaminopropionic acid; it was crystallized from methyl alcohol in the form of fine, colorless, lustrous needles, which are slightly soluble in water, ether, and benzene, and quite soluble in methyl and ethyl alcohol.

4.3 g of cinnamic acid, with a m. p. of 133° was extracted from the ether solution after working in the usual way, and recrystallization from water. A mixture test with pure cinnamic acid did not give a depression of the melting point.

b) A mixture of 3.52 g (0.032 mole) of benzylamine, 3.5 g (0.033 mole) of benzaldehyde, 3.45 g (0.033 mole) of malonic acid, and 20 ml of dry benzene were gently heated in a flask with a descending condenser, over a water bath at 60.65° for 2.5 hours; toward the end, the temperature was raised and held for half an hour at 70°. Thereupon a large quantity of a white, flaky substance was precipitated out; the precipitate was separated, washed several times with anhydrous ether and dried. The yield was 60 g (61%) the m. p. was 127-129° (with decomposition).

After recrystallization from anhydrous alcohol at a temperature of 60-70°, 3.06 g (31%) of a substance with a m. p. of 138-140° was obtained.

4.71 mg sub.: 11.87 mg CO_2; 2.39 mg H_2O. 4.10 mg sub.: 10.31 mg CO_2; 2.12 mg H_2O. 4.76 mg sub.: 0.199 ml N_2 (25°, 754 mm). 5.98 mg sub.: 0.254 ml N_2 (25°, 754 mm). Found %: C 68.77, 68.72; H 5.68, 5.79; N 4.75, 4.83. $C_{17}H_{17}O_4N$. Calculated %: C 68.2; H 5.68; N 4.68.

The substance which was isolated was, evidently, an intermediate product which was formed on the interaction of benzylamine, benzaldehyde, and malonic acid; it was crystallized in the form of colorless, lustrous plates, which were difficultly soluble in water, ether, benzene, and cold alcohol, and quite soluble in hot alcohol.

The preparation of the carboethyoxy derivative of β-phenyl-β,N-methylaminopropionic acid. To 1.12 g (0.006 mole β-phenyl-β,N-methylaminopropionic acid with a m. p. of 168°, dissolved in 10 ml of a 10% solution of potassium hydroxide (three times as much), was added over a period of 20 minutes, with mechanical stirring and cooling down to 0°, 0.65 ml of the ethyl ester of chlorocarbonic acid (excess 10%).

The solution was mixed for 1 hour with cooling, then for one hour at room temperature. The solution was again cooled to 0° and acidified with hydrochloric acid (1:1) until it gave an acid reaction on a Congo red indicator. First an oil precipitated, which began to crystallize in the form of course, white crystals; the latter were separated, washed, and dried. The yield was 1.01 g (64.3%) of a carboethoxy derivative with a m. p. of 76-78°. After recrystallization from a mixture of ether and petroleum ether 0.9 g of the carboethoxy derivative with a m. p. of 77-78° was isolated; it crystallized in the form of coarse plates.

6.16 mg sub.: 14.09 mg CO_2; 3.80 mg H_2O. 4.17 mg sub.: 9.52 mg CO_2; 2.59 mg H_2O. 7.71 mg sub.: 0.389 ml N_2 (20.5°, 752 mm). 6.18 mg sub.: 0.320 ml N_2 (20.5°, 752 mm). Found %: C 62.42, 62.30; H 6.90, 6.95, N 5.81, 5.96. $C_{13}H_{17}O_3N$. Calculated %: C 62.16; H 6.77; N 5.58.

The obtained compound is a carboethoxy derivative of β-phenyl β,N-methylaminopropionic acid; it is quite soluble in the ordinary organic solvents: ether, alcohol, benzene, acetone; it is less soluble in petroleum ether.

The obtaining of the carboethoxy derivative of α-ethyl-β-phenyl-β,N-methylaminopropionic acid. To 0.9 g (0.004 mole) of α-ethyl-β-phenyl-β,N-methylaminopropionic acid with a m. p. of 205-206° dissolved in 10 ml

of a 10% solution of potassium hydroxide, was added gradually from a graduated pipet over the course of 20 minutes (with mechanical stirring and cooling of the solution to −1°), 0.46 ml of the ethyl ester of chlorocarbonic acid (10% excess). On the addition of the chlorocarbonic ester, the solution was mixed for an hour with cooling, and then, for one more hour, at room temperature. The solution was first cooled to 0° and acidified with hydrochloric acid (1:1) until it showed an acid reaction with a Congo red indicator. An oil was precipitated, and on standing, began to crystallize. The yield was 0.97 g (80%); the m. p. was 114-117°. After recrystallization from a mixture of ether and petroleum ether, 0.9 g of a substance with a m. p. of 117-118° was obtained in the form of fine, colorless needles.

4.70 mg sub.: 11.12 mg CO_2; 3.20 mg H_2O. 6.39 mg sub.: 15.07 mg CO_2; 4.43 mg H_2O. 7.60 mg sub.: 0.331 ml N_2 (21.5°, 750 mm). 5.98 mg sub.: 0.266 ml N_2 (21.5°, 750 mm). Found %: C 64.56, 64.36; H 7.62, 7.75; N 4.98, 5.09. $C_{15}H_{21}O_4N$. Calculated %: C 64.51; H 7.53; N 5.02.

The obtained compound is a carboethoxy derivative of α-benzyl-β-phenyl-β,N-methylaminopropionic acid; it is quite soluble in alcohol, ether, benzene, and acetone, and slightly soluble in water and petroleum ether.

The preparation of the carboethoxy derivative of α-benzyl-β-phenyl-β,N-methylaminopropionic acid. In a three-necked bottle, equipped with a mechanical stirrer, a thermometer, and a graduated pipet, was placed 18 ml of a 10% solution of potassium hydroxide; 2.58 g of α-benzyl-β-phenyl-β,N-methylaminopropionic acid with a m. p. of 218° was added. The solution was cooled to −2°, and 1.0 ml of the ethyl ester of chlorocarbonic acid (10% excess) was added gradually over a period of 30 minutes, with constant stirring of the solution, and with the temperature kept in the interval from 0 to +3°. The mixing was continued for 1 hour with cooling of the solution, and then for 1.5 hours at room temperature. The solution was first cooled to 0° and gently acidified with hydrochloric acid (1:1) until it gave an acid reaction with a Congo red indicator; the white residue, which was separated, was allowed to stand until the following day in order to achieve better crystallization. Then the precipitate was isolated, washed with a water, and dried. The yield was 3.07 g. After recrystallization from aqueous alcohol 2.85 g (87%) of a substance with a m. p. of 139-141° was obtained. After two recrystallizations from aqueous alcohol, the m. p. was 139.5-141°.

4.92 mg sub.: 12.67 mg CO_2; 2.90 mg H_2O. 4.54 mg sub.: 11.68 mg CO_2; 2.74 mg H_2O. 7.256 mg sub.: 0.260 ml N_2 (22°, 750 mm). 4.721 mg sub.: 0.159 ml N_2 (22°, 749 mm). Found %: C 70.27, 70.21; H 6.59, 6.75; N 4.09, 3.83. $C_{20}H_{23}O_4N$. Calculated %: C 70.38; H 6.74; N 4.10.

The synthesized substance is a carboethoxy derivative of α-benzyl-β-phenyl-β,N-methylaminopropionic acid; it is quite soluble in ether, benzene, and alcohol, and difficultly soluble in water and petroleum ether.

β-Phenyl-β,N-1-methylureidopropionic acid*. 1.37 g (0.007 mole) of β-phenyl-β,N-methylaminopropionic acid with a m. p. of 167-168°, 0.70 g of potassium cyanate, and 7.5 ml of water were heated in a flask equipped with a reflux condenser for 2.5 hours over a boiling water bath. On the completion of the heating, the solution was filtered in order to rid it of the small amount of impurities present, cooled to 0°, and gently acidified with hydrochloric acid (1:1) until it gave an acid reaction to a Congo red indicator.

The white, flaky precipitate which was separated was allowed to stand for several hours, filtered, washed successively with water and ether, and dried. The yield was 1.13 g (66.5%) of β-phenyl-βN-methylureidopropionic acid with a m. p. of 165°. After recrystallization from alcohol the m. p. was 165-167° (Johnson gives m. p. 165-167°.

α-Ethyl-β-phenyl-β,N-1-methylureidopropionic acid. 0.8 g (0.0038 mole) of α-ethyl-β-phenyl-β,N-methylaminopropionic acid with a m. p. of 205-206°, 0.34 g of potassium cyanate (10% excess), and 10 ml of water were heated in a flask equipped with a reflux condenser for 2 hours and 40 minutes over a boiling water bath. On the completion of the heating, the solution was cooled, filtered to remove the small amount of admixtures, again cooled to 0° and acidified with hydrochloric acid (1:1) until an acid reaction was given with Congo red indicator. The white, flaky precipitate which separated is allowed to stand until the next day for better crystallization, and then filtered, washed first with water, then with ether, and dried. The yield was 0.9 g (93%), the m. p. was 202°. After recrystallization from alcohol, 0.52 g (53.9%) of a substance with an m. p. of 208° was isolated. A mixed sample of the obtained substance with α-ethyl-β-phenyl-β,N-methylaminopropionic acid gave a depression of the melting point (m. p. 175-180°).

* Obtained first by Evans and Johnson [5], but the conditions under which the experiment was carried out were not described in detail.

4.54 mg sub.: 0.423 ml N_2 (19.5°, 761 mm). 4.50 mg sub.: 0.422 ml N_2 (19°, 762 mm). Found %: N 10.88, 10.99. $C_{13}H_{18}O_3N_2$. Calculated %: N 11.20.

The synthesized substance is α-ethyl-β-phenyl-β,N-1-methylureidopropionic acid, which is crystallized in the form of fine, colorless needles, difficultly soluble in ether, benzene, and cold water, and quite soluble in alcohol.

α-n-Butyl-β-phenyl-β,N-1-methylureidopropionic acid. 1.0 g (0.004 mole) of α-n-butyl-β-phenyl-β, N-methylaminopropionic acid with a m. p. of 183°, 0.64 g (0.008 mole) of potassium isocyanate (excess 88%), and 10 ml of water were heated in a flask equipped with a reflux condenser for 4.5 hours over a boiling water bath. It should be pointed out that in the very first ten minutes of the heating the entire precipitate went into solution. On the completion of heating, the solution was cooled, filtered to remove the small quantity of impurities, again cooled to 0° and acidified with hydrochloric acid (1:1) until it gave an acid reaction with a Congo red indicator. The precipitate which was isolated was allowed to stand until the following day in order to improve the crystallization, then it was filtered, and washed several times with water and ether. The yield was 0.73 g, the m. p. was 205°. After two recrystallizations from alcohol, 0.58 g of a substance with m. p. of 213-214° was isolated; the yield was 74%, calculated on the butylamino acid which entered into the reaction. A mixed sample of the obtained substance with the original α-n-butyl-β-phenyl-β,N-methylaminopropionic acid gave a sharp depression of the melting point (m. p. 167-170°).

4.57 mg sub.: 0.401 ml N_2 (21.5°, 755 mm). 5.23 mg sub.: 0.467 ml N_2 (21.5°, 755 mm). Found %: N 10.10, 10.28. $C_{15}H_{22}O_3N_2$. Calculated %: N 10.07.

The synthesized substance is α-n-butyl-β-phenyl-β-N-1-methylureidopropionic acid. After acidification with hydrochloric acid, the solution was concentrated, and, on cooling, a 10% solution of potassium hydroxide was added; then the amino acid which had not entered into the reaction was precipitated with acetic acid. The white, flaky precipitate which was separated was filtered and washed with water and anhydrous ether.

After recrystallization from alcohol, 0.34 g of α-n-butyl-β-phenyl-β,N-methylaminopropionic acid with a m. p. of 182-183° was obtained. A mixed sample of this substance with pure α-n-butyl-β-phenyl-β,N-methylaminopropionic acid did not give a depression of the melting point.

3-N-methyl-4-phenyldihydrouracil*. 0.5 g (0.002 mole) of β-phenyl-β,N-1-methylureidopropionic acid (m. p. 165-167°) and 10 ml of 12% hydrochloric acid were boiled in a flask with a reflux condenser for two hours on a grid. On the completion of the heating, the solution was filtered and cooled; white, lustrous crystals were separated and filtered, washed with water, ether, and dried. The yield was 0.38 g (83%) of 3-N-methyl-4-phenyl-dihydrouracil with a m. p. of 163-164°.

After recrystallization from alcohol, 0.3 g of the dihydrouracil with a m. p. of 164-165° was isolated in the form of long, lustrous needles. After two recrystallizations from alcohol, the substance melted at 164-165°. A mixed sample of the obtained dihydrouracil with the original ureido acid had a melting point of 151-155°.

Since the m. p. of the 3-N-methyl-4-phenyldihydrouracil synthesized by Johnson differed from that obtained by us (Johnson gives 158-159.5°), a full analysis of the substance with a m. p. of 164-165° was carried out.

4.98 mg sub.: 11.81 mg CO_2; 2.53 mg H_2O. 5.07 mg sub.: 12.04 mg CO_2; 2.55 mg H_2O. 6.49 mg sub.: 0.775 ml N_2 (21°, 755 mm). 5.59 mg sub.: 0.671 ml N_2 (21°, 755 mm). Found %: C 64.72, 64.81; H 5.68; 5.63; N 13.82, 13.89. $C_{11}H_{12}O_2N_2$. Calculated %: C 64.70; H 5.88; N 13.72.

The obtained substance is 3-N-methyl-4-phenyldihydrouracil.

3-N-Methyl-4-phenyl-5-ethyldihydrouracil. 0.3 g (0.001 mole) of α-ethyl-β-phenyl-β,N-1-methylureidopropionic acid with a m. p. of 208° and 8 ml of 12% hydrochloric acid were boiled in a flask with a reflux condenser on a grid of 2.5 hours. In the first ten minutes of heating, all of the ureido acid was dissolved. On the completion of the heating, the solution was filtered, cooled; thereupon fine, lustrous crystals were precipitated out. In order to achieve full crystallization, the precipitate was allowed to stand for several hours. The crystals which were isolated were filtered, washed with water, and then several times with ether. The yield was 0.25 g (90%), the m. p. was 137°. After recrystallization from alcohol the substance melted at 137-138°.

* First prepared by Evans and Johnson [5] but the conditions of conducting of the experiment were not described in detail.

5.13 mg sub.: 12.66 mg CO_2; 3.18 mg H_2O. 4.83 mg sub.: 11.93 mg CO_2; 3.02 mg H_2O. 4.31 mg sub.: 0.463 ml N_2 (22.5°, 747 mm). 5.69 mg sub.: 0.605 ml N_2 (22.5°, 747 mm). Found %: C 67.34, 67.41; H 6.93, 7.00; N 12.20, 12.07. $C_{13}H_{16}O_2N_2$. Calculated %: C 67.24; H 6.89; N 12.06.

The obtained substance was 3-N-methyl-4-phenyl-5-ethyldihydrouracil; it is difficultly soluble in water, ether, and benzene, and is quite soluble in alcohol.

3-N-Methyl-4-phenyl-5-n-butyldihydrouracil. 0.58 g (0.002 mole) of α-n-butyl-β-phenyl-β,N-1-methylureidopropionic acid with a m. p. of 213-214° and 15 ml of 12% hydrochloric acid were heated in a round-bottomed flask with a reflux condenser on a grid for one hour; thereupon, the precipitate was not dissolved; 5 ml more of hydrochloric acid (1:1) was added and the mixture was boiled for 3 more hours. On the completion of the heating, the solution was cooled; thereupon, white crystals were isolated. The precipitate was filtered, washed with water, and then several times with anhydrous ether. The yield was 0.52 g, the m. p. was 192-194°. After recrystallization from a mixture of alcohol and anhydrous ether, 0.45 g (83%) of a substance with a m. p. of 195-197° was isolated. A mixed sample of the obtained substance with pure α-n-butyl-β-phenyl-β,N-1-methylureidopropionic acid gave a depression of the melting point (m. p. 183-187°).

After two recrystallizations from alcohol, the substance had a m. p. of 197.5-199°.

5.65 mg sub.: 14.34 mg CO_2; 3.82 mg H_2O. 5.38 mg sub.: 13.68 mg CO_2; 3.58 mg H_2O. 6.77 mg sub.: 0.637 ml N_2 (20.5°, 751 mm). 6.19 mg sub.: 0.576 ml N_2 (20.5°, 751 mm). Found %: C 69.26, 69.39, H 7.56, 7.44; N 10.81, 10.70. $C_{15}H_{20}O_2N_2$. Calculated %: C 69.23; H 7.69; N 10.77.

The obtained compound is 3-N-methyl-4-phenyl-5-n-butyldihydrouracil, which crystallizes from alcohol in the form of fine, colorless needles; it is difficultly soluble in the common organic solvents, and quite soluble in hot alcohol; it is insoluble in water and mineral acids.

SUMMARY

1. The following α-alkyl-β-phenyl-β,N-alkylaminopropionic acids have been synthesized by the addition of alkylmalonic acids to Schiff's base: α-ethyl-β-phenyl-β,N-methylaminopropionic, α-n-butyl-β-phenyl-β,N-methylaminopropionic, and β-phenyl-β,N-benzylaminopropionic acids.

This creates the basis for the confirmation of the correctness of the first scheme of the formation of β-amino acids.

2. It has been established that the alkylated β-amino acids are obtained in two diastereoisomeric forms.*

3. Carboethoxy derivatives of the following acids have been prepared: β-phenyl-β,N-methylaminopropionic, α-ethyl-β-phenyl-β,N-methylaminopropionic, and α-benzyl-β-phenyl-β,N-methylaminopropionic.

4. The following new ureido acids have been isolated: α-ethyl-β-phenyl-β,N-1-methylureidopropionic and α-n-butyl-β-phenyl-β,N-1-methylureidopropionic.

5. The following new alkylated dihydrouracils have been prepared, by means of the closing of the pyrimidine ring, from the corresponding alkylated β-ureido acids: 3-N-methyl-4-phenyl-5-ethyl- and 3-N-methyl-4-phenyl-5-n-butyl-dihydrouracils.

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THE REACTIONS OF TRICHLOROPHOSPHAZOSULFONARYLS WITH PHENOLS AND THE AROMATIC ESTERS OF ARYLSULFONAMIDOPHOSPHORIC ACIDS

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Trichlorophosphazosulfonaryls, like phosphorus oxychloride [1], react with phenols with considerably more difficulty than with alcohols [2]. On the interaction of trichlorophosphazosulfonphenyl with phenol, the evolution of hydrogen chloride just barely begins at 100°, and on the interaction of phenol with α-trichlorophosphazosulfonnaphthylit does not begin until 140-150°.

The reaction of trichlorophosphazosulfonaryls with sodium phenolate takes place incomparably more easily. The reaction occurs according to the scheme:

$$ArSO_2N=PCl_3 + 3C_6H_5ONa \rightarrow 3NaCl + ArSO_2N=P(OC_6H_5)_3,$$

that is, with the formation of the triphenyl ester of the arylsulfonimidophosphoric acids.

Thus, the following triphenyl esters were prepared:

$ArSO_2N=P(OC_6H_5)_3$, where: Ar = C_6H_5, o-$CH_3C_6H_4$, α-$C_{10}H_7$ and β-$C_{10}H_7$.

The triphenyl esters of the arylsulfonimidophosphoric acids are colorless, odorless and tasteless crystalline substances. Chemically, the full phenyl esters of the arylsulfonimidophosphoric acids are stable, neutral substances. They, like the trialkyl esters [2], are fully stable to the action of water, and do not react with it even on prolonged boiling. They are also stable against the action of dilute aqueous solutions of mineral acids and bases.

The stability of the triphenyl esters of the arylsulfonimidophosphoric acids to the action of dilute aqueous solutions of sodium hydroxide is explained by their insolubility in water. In an aqueous alcohol solution of sodium hydroide, in which the triphenyl esters are quite soluble, saponification takes place easily and quickly, with the formation of the sodium salts of the diphenyl esters of the arylsulfonamidophosphoric acids, $ArSO_2NNaPO(OC_6H_5)_2$.

Longer heating of the triphenyl esters with a 0.2 N water-alcohol solution of sodium hydroxide does not lead to further saponification; hydrolysis stops with the formation of the sodium salts of the diphenyl esters. In relation to dilute mineral acids, the triphenyl esters of arylsulfonimidophosphoric acids are more stable than they are in relation to bases. However, the stability of the full phenyl esters of the arylsulfonimidophosphoric acids to the action of weak solutions of mineral acids cannot be explained only by their insolubility in water.

The main products of the hydrolysis of the arylsulfonimidophosphoric acids with a 0.2 N water-alcohol solution of hydrochloric acid are the diphenyl esters, which are formed according to the scheme:

$$ArSO_2N=P(OC_6H_5)_3 + H_2O \rightarrow ArSO_2NHPO(OC_6H_5)_2 + C_6H_5OH.$$

The diphenyl esters of our more stable triphenyl esters were also saponified only under more rigid conditions.

The quantitative data on the hydrolysis of the triphenyl esters of arylsulfonimidophosphoric acids through the use of acids, given in the experimental section of this paper, are only approximate, since the quantitative analysis of the mixture of products formed is very difficult to carry out without losses of material. However, for the qualitative characteristics, the obtained data are fully satisfactory.

The diphenyl esters of arylsulfonamidophosphoric acids, like the dialkyl esters [2] are also easily prepared with good yields from the dichloroanhydrides of the arylsulfonamidophosphoric acids and sodium phenolate. The reaction of sodium phenolate with the dichloroanhydrides in the presence of a solvent (benzene) takes place just as easily as with the trichlorophosphazosulfonaryls, according to the scheme:

$$ArSO_2NHPOCl_2 + 3C_6H_5ONa \rightarrow ArSO_2NNaPO(OC_6H_5)_2 + C_6H_5OH + 2NaCl.$$

The sodium salts which have been formed remain in the benzene solution for some time after the completion of the reaction. On the heating of the reaction mixture to boiling, they precipitate out in the solid state. An exception is the sodium salt of the diphenyl ester of phenylsulfonamidophosphoric acid, the benzene solution of which is quite stable. The reaction mixture of Na phenolate with the dichloroanhydride of phenylsulfonamidophosphoric acid in a benzene medium is a homogeneous, clear solution, containing a slimy sodium chloride precipitate on the bottom. However, the dried, crystalline sodium salt of the diphenyl ester of phenylsulfonamidophosphoric acid, is insoluble in benzene.

Attention is attracted to the character of the course of reaction of Na phenolate with the dichloroanhydride of o-tolylsulfonamidophosphoric acid. The reaction mixture, consisting of powdered Na phenolate, finely ground dichloroanhydride, and benzene, on being shaken up, sets at first into a porous, spongy mass; then the mixture begins to warm up (to 50-60°), and the spongy mass goes into solution. Evidently, some intermediate product is first formed, then the reaction takes place according to the scheme given above.

The following diphenyl esters were obtained by the reaction of the dichloroanhydrides of the arylsulfonamidophosphoric acids with sodium phenolate:

$$ArSO_2NHPO(OC_6H_5)_2,$$ where $Ar = C_6H_5$, o-$CH_3C_6H_4$, α-$C_{10}H_7$ and β-$C_{10}H_7$.

The diphenyl esters of the arylsulfonamidophosphoric acids are colorless, crystalline substances with comparatively high melting points (138-179°).

Chemically, the diphenyl esters are mono-basic acids, which are titrated by one equivalent of a sodium hydroxide solution (with phenolphthalein).

The diphenyl esters of phenylsulfonamidophosphoric acids are very stable in relation to the action of dilute acids and bases.

Under more rigorous conditions (see Experimental section), the diphenyl esters are saponified with the formation of the corresponding sulfamides.

The o-, m-, and p-cresyl esters were prepared in an analogous manner to the preparation of the phenyl esters. Sodium cresolates react with trichlorophosphazosulfonaryls just as easily as sodium phenolates. There is no essential difference in the method of separation of the reaction products, or in the method of carrying out the reaction itself.

The tricresyl esters of phenylsulfonimidophosphoric acid were prepared:

$$C_6H_5SO_2N=P(OAr)_3,$$ where Ar = o-, m-, and p-$CH_3C_6H_4$;

those of α-naphthylsulfonimidophosphoric acid:

$$\alpha\text{-}C_{10}H_7SO_2N=P(OAr)_3,$$ where Ar = o- and p-$CH_3C_6H_4$

and the p-tricresyl ester of o-tolylsulfonimidophosphoric acid:

$$o\text{-}CH_3C_6H_4SO_2N=P(OC_6H_4CH_3\text{-}p)_3.$$

The tricresyl esters, with the exception of the o-tricresyl ester of phenylsulfonimidophosphoric acid, are thick, oily liquids. They did not crystallize either on long standing (over a year), or on cooling in a mixture of snow and salt. The liquid tricresyl esters were not obtained in the chemically pure state, since they could not be distilled without decomposition.

Chemically, the tricresyl esters are similar to the full phenyl esters. They, like the phenyl esters, are not hydrolyzed by water and dilute aqueous solutions of mineral acids and bases. A water-alcohol solution of sodium hydroxide easily saponifies the tricresyl esters, with the formation of the sodium salts of the dicresyl esters.

The m-dicresyl ester of phenylsulfonamidophosphoric acid, $C_6H_5SO_2NHPO(OC_6H_4CH_3\text{-}m)_2$, the p-dicresyl ester of o-tolylsulfonamidophosphoric acid

$$o\text{-}CH_3C_6H_4SO_2NHPO(OC_6H_4CH_3\text{-}p)_2$$

and the o-dicresyl ester of α-naphthylsulfonamidophosphoric acid

$$\alpha\text{-}C_{10}H_7SO_2NHPO(OC_6H_4CH_3\text{-}o)_2$$

and the p-dicresyl ester of α-naphthylsulfonamidophosphoric acid

$$\alpha\text{-}C_{10}H_7SO_2NHPO(OC_6H_4CH_3\text{-}p)_2,$$

were prepared by the hydrolysis of the tricresyl esters with a water-alcohol solution of sodium hydroxide.

The dicresyl esters of phenylsulfonamidophosphoric acids, like the diphenyl esters, are easily prepared with good yields from the dichloroanhydrides of the arylsulfonamidophosphoric acids and sodium cresolates. The dicresyl esters of phenylsulfonamidophosphoric acid:

$$C_6H_5SO_2NHPO(OAr)_2 \text{ where } Ar = o\text{-, m- and } p\text{-}CH_3C_6H_4$$

and the p-dicresyl esters:

$$ArSO_2NHPO(OC_6H_4CH_3\text{-}p), \text{ where } Ar = CH_3C_6H_4\text{-}o,\ \alpha\text{-}C_{10}H_7 \text{ and } \beta\text{-}C_{10}H_7$$

were prepared by the reactions of the sodium cresolates with the dichloroanhydrides.

The dicresyl esters of the arylsulfonamidophosphoric acids are crystalline substances, which crystallize in well-formed crystals from carbon tetrachloride or alcohol.

The dicresyl esters are insoluble in water. All of the dicresyl and diphenyl esters have a very bitter taste (compare with dibutyl esters [2]).

Chemically the dicresyl esters are mono-basic acids, which are titrated with one equivalent of a sodium hydroxide solution (to phenolphthalein). Exactly like the diphenyl esters, they are stable against the action of dilute solutions of mineral acids, and bases.

It would be interesting to prepare the full phenyl esters of the arylsulfonamidophosphoric acids, which would contain in the phenyl ring some strong electronegative group, e. g. NO_2.

The nitrophenyl esters of the arylsulfonimidophosphoric acids were prepared by the reaction of the trichlorophosphazosulfonaryls with sodium o-nitrophenolate; these nitrophenyl esters differ sharply in their properties from the corresponding phenyl esters.

The reaction of sodium o-nitrophenolate with the trichlorophosphazosulfonaryls takes place with difficultly, upon long heating, according to the scheme:

$$ArSO_2N{=}PCl_3 + 3NaOC_6H_4NO_2 \rightarrow 3NaCl + ArSO_2N{=}P(OC_6H_4NO_2)_3;$$

this is even more true of its reaction with the dichloroanhydrides of the arylsulfonamidophosphoric acids.

The trinitrotriphenyl esters, unlike the triphenyl esters, are very easily hydrolyzed by water; it is therefore necessary to use completely dry solvents during their isolation and purification.

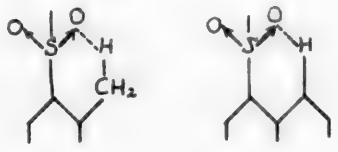
Thus, the o-trinitrotriphenyl esters were prepared

$$ArSO_2N{=}P(OC_6H_4NO_2\text{-}o)_3, \text{ where } Ar = C_6H_5,\ o\text{-}CH_3C_6H_4 \text{ and } \alpha\text{-}C_{10}H_7.$$

The trinitrotriphenyl esters are crystalline substances, yellow in color, with the odor of nitrophenol. They are quite soluble in hot benzene, acetone, hot alcohol, and are insoluble in ether and water. They crystallize from benzene as well-formed, clear, yellow prisms.

Our attention is attracted to the high melting points of the full nitrophenyl esters of o-tolyl- and α-naphthyl-sulfonimidophosphoric acids (152 and 148°). All of the other full esters, prepared or described in this paper, are either liquids, or crystalline substances which melt at temperatures not higher than 95°.

It is very probable that the comparatively high melting points of the o-tolyl- and α-naphthyl derivatives are explained by the fact that these compounds have identical characteristic structural details; namely, in both of these types of compounds, the o-position in the nucleus in relation to the sulfo group, is substituted, and has the possibility of the formation of a hydrogen bond with the atom of oxygen linked with the sulfur,



Therefore, the full esters of o-tolylsulfonimidophosphoric acids, in comparison with the corresponding esters of phenyl- and p-tolylsulfonimidophosphoric acids, have higher melting points, crystallize better, and are somewhat less soluble. In this relationship, the esters of o-tolylsulfonimidophosphoric acids are more similar to the corresponding derivatives of α-naphthylsulfonimidophosphoric acids than to the phenyl or p-tolyl derivatives.

In their chemical properties (the great ease of hydrolysis), the full nitrophenyl esters are more similar to the mixed anhydrides than to the esters. On dissolution in 96% alcohol, they are immediately hydrolyzed with the formation of nitrophenol and the dinitrophenyl ester of arylsulfonamidophosphoric acid, according to the scheme:

$$ArSO_2N=P(OC_6H_4NO_2\text{-}o)_3 + H_2O \rightarrow ArSO_2NHPO(OC_6H_4NO_2\text{-}o)_2 + HOC_6H_4NO_2.$$

In relation to the moisture of the air, for comparatively short periods, the crystals of the full nitrophenol esters are quite stable. However, on long standing in the air, they slowly decompose. Thus, on the storing of pure trinitrotriphenyl esters in flasks that were not tightly covered over a period of a year, small admixtures of regular crystals, which melted at 45° and did not give a depression of the melting point with o-nitrophenol, were detected. It is interesting that the o-nitrophenol which was isolated on long standing was not distributed evenly throughout the entire mass of the trinitrotriphenyl ester, but was concentrated in separate places in the form of well-formed clear crystals, which increased in size as the length of time of storage increased. This is explained, probably, by the great volitility of o-nitrophenol at room temperature.

On heating with water, the full nitrophenyl esters are hydrolyzed more slowly than in alcohol solutions, which is probably explained by their lower solubility in water.

The dinitrodiphenyl esters of the arylsulfonamidophosphoric acids were also prepared by the reaction of sodium o-nitrophenolate with the dichloroanhydrides of the corresponding acids. The dichloroanhydrides of the arylsulfonamidophosphoric acids react with sodium o-nitrophenolate with great difficulty. In order to prepare the dinitrodiphenyl esters of phenyl- and o-tolylsulfonamidophosphoric acids, a mixture consisting of sodium o-nitrophenolate, the dichloroanhydride of the acid, and benzene is heated to boiling for 20 hours. Even with this treatment, the reaction does not take place completely. On the heating of the dichloroanhydride of α-naphthylsulfonamidophosphoric acid with sodium o-nitrophenolate in boiling benzene for 50 hours, only a small part of the original substances enter into the reaction.

The dinitrodiphenyl esters were prepared by the reaction of the dichloroanhydrides with sodium o-nitrophenolate:

$$ArSO_2NHPO(OC_6H_4NO_2\text{-}o)_2, \text{ where } Ar = C_6H_5 \text{ and } o\text{-}CH_3C_6H_4.$$

It is more convenient to prepare the dinitrodiphenyl ester of α-naphthylsulfonamidophosphoric acid, $\alpha\text{-}C_{10}H_7SO_2NHPO(OC_6H_4NO_2\text{-}o)_2$, from the corresponding full nitrophenyl ester on its dissolution in alcohol.

The dinitrodiphenyl esters of the arylsulfonamidophosphoric acids are colorless crystalline substances, which crystallize well from alcohol.

The dinitrodiphenyl esters are mono-basic acids. They are titrated by one equivalent of sodium hydroxide (with phenolphthalein). They are stable in relation to water, not hydrolyzing to any considerable extent even on long boiling with water, but they are easily hydrolyzed on heating with a normal solution of sodium hydroxide

EXPERIMENTAL

The preparation of the triphenyl esters of arylsulfonimidophosphoric acids. In a flask, with a volume of 150-200 ml, were placed 0.06 mole (7.0 g) of dry, finely ground sodium phenolate, and 10 ml of dry benzene; a solution of 0.02 mole of trichlorophosphazosulfonaryl in 40 ml of benzene was added with constant stirring. In the case of trichlorophosphazosulfonphenyl and o-tolyl, the reaction takes place easily on the warning of the reaction mixture to 50-60°. The sodium phenolate quickly disappears and a slimy sodium chloride precipitate is formed. For the completion of the reaction, the flask is fastened to a reflux condenser and the mixture is heated over a boiling water bath for 30 minutes.

In the case of α- and β-trichlorophosphazosulfonaphthyls, the reaction takes place slowly with a small amount of heat. In order to carry out the reaction, the reaction mixture is heated to boiling for 1 hour. The sodium phenolate is sometimes whipped into a clot which becomes covered with sodium chloride; this slows down the reaction a great deal, or causes it to stop entirely. It is helpful to break up the sodium phenolate clot which has been formed, with a glass rod.

After the completion of the reaction, the sodium chloride is drawn off, and the filtrate is evaporated in a vacuum over a boiling water bath until all of the solvent has been driven off. The residue, which is damp triphenyl ester, is either crystallized immediately, or is first worked with a 0.05 N solution of sodium hydroxide. In the latter case, the pure products are ordinarily obtained after only one crystallization.

The triphenyl esters are easily dissolved in dioxane, acetone, chloroform, benzene, hot alcohol, and hot carbon tetrachloride, and dissolved with more difficulty in ether.

For the triphenyl ester of phenylsulfonimidophosphoric acid, the yield was 8.50 g (91.4%). It is difficultly soluble in petroleum ether. It crystallizes well from alcohol, carbon tetrachloride, and petroleum ether. The prisms (from alcohol) have a melting point of 85-86°.

Found %: N 2.98, 2.90. $C_{24}H_{20}O_5NSP$. Calculated %: N 3.01.

For the triphenyl ester of o-tolylsulfonimidophosphoric acid the yield was 7.52 g (78.5%).

The small prism (from alcohol) had a melting point of 79-80°.

Found %: N 3.03, 2.96. $C_{25}H_{22}O_5NSP$. Calculated %: N 2.92.

For the triphenyl ester of β-naphthylsulfonimidophosphoric acid the yield was 7.93 g (77.0%). They were difficultly soluble in petroleum ether, and insoluble in water. The prisms (from carbon tetrachloride or alcohol) had a melting point of 94-95°.

Found %: N 2.74, 2.84. $C_{28}H_{22}O_5NSP$. Calculated %: N 2.72.

For the triphenyl ester of β-naphthylsulfonimidophosphoric acid the yield was 8.61 g (83.6%). It was insoluble in water and petroleum ether. The melting point of the small prisms (from alcohol or carbon tetrachloride) was 90-91°.

Found %: N 2.70, 2.81. $C_{28}H_{22}O_5NSP$. Calculated %: N 2.72.

The hydrolysis of the triphenyl esters of the arylsulfonimidophosphoric acids with alcohol solutions of sodium hydroxide. In a small flask, with a volume of 50 ml, equipped with a reflux condenser, were placed 0.001 mole of the full phenyl ester of the arylsulfonimidophosphoric acid, and 5 ml of a 1.0 N solution of sodium hydroxide and 20 ml of alcohol were added. The mixture was heated over a boiling water bath for 1 hour, after which the alcohol was distilled off in a vacuum. The residue, after the alcohol was driven off, dissolved completely in water, and thus did not contain triphenyl ester. After the acidification of the solution with hydrochloric or sulfuric acid until it gave an acid reaction with a Congo red indicator, the diphenyl esters were precipitated in the form of thick oil, which was easily crystallized on being stirred slightly with a glass rod. The precipitate was filtered with suction, washed well with water and dried. The diphenyl ethers obtained in this way have a clear melting point. A mixed sample with diphenyl esters obtained from the dichloranhydrides of the arylsulfonamidophosphoric acids and sodium phenolate, did not give a depression of the melting point. The yield of the diphenyl esters of the arylsulfonamidophosphoric acids obtained by alkaline hydrolysis, varied between 90.9 and 96.5%;

The hydrolysis of the triphenyl esters of arylsulfonimidophosphoric acids by an alcohol solution of hydrochloric acid. 0.01 g-mole of the triphenyl ester of arylsulfonimidophosphoric acid was placed in a 500 ml flask equipped with a reflux condenser; 200 ml of alcohol and 50 ml of a 1.0 N aqueous solution of hydrochloric acid was added. The mixture was heated to boiling for one hour. After the distilling off of the alcohol in a vacuum, a heavy oily layer was formed which was not soluble in water. The acidified, aqueous solution was decanted and discarded and the oily layer was washed with water. Ten ml of a 1.0 N solution of sodium hydroxide was added to the oily residue. They were well washed and the oil which was not dissolved was washed with water. After the first washing, the oily liquid ordinarily begins to crystallize. The crystalline precipitate which consists of that part of the triphenyl ester which has not reacted, and a small quantity of admixtures, is dried and crystallized. The yield is from 56.1% to 62.5%. The alkaline solution and the wash water are mixed and filtered. After acidification with hydrochloric acid until the solution gives an acid reaction to a Congo red indicator, a crystalline precipitate is formed; this precipitate is the diphenyl ester. The diphenyl ester is separated, washed, and dried. Its melting point differs by 1-2° from that of the pure substance. The yield is from 16.6% to 18.0%.

The preparation of the diphenyl esters of arylsulfonamidophosphoric acids. 50 ml of benzene was added with stirring to a mixture consisting of 0.02 mole of the dichloroanhydride of an arylsulfonamidophosphoric acid, finely ground, and 0.06 -mole of sodium phenolate. The reaction takes place gently with little evolution of heat. The sodium salts of the diphenyl esters, formed as a result of the reaction, remain in solution, but on the heating of the

reaction mixture to boiling, they are precipitated in the crystalline state. The reaction mixture is evaporated until dry, the solvent is distilled off in a vacuum over a boiling water bath. 200 ml of water is added to the residue and the mixture is agitated until the residue dissolves. (The sodium salt of the diphenyl ester of α-naphthylsulfonamidophosphoric acid is difficultly soluble in cold water. For solution, it is necessary to gently heat the mixture. In hot water the salt is dissolved very easily.) The solutions of the sodium salts are acidified with a 2.0 N solution of sulfuric or hydrochloric acid until they give an acid reaction with a Congo red indicator. The diphenyl esters are difficultly soluble in water and precipitate from an acidified solution in the form of a thick, viscous mass which is easily and completely crystallized. The diphenyl esters which have been crystallized are filtered with suction, washed with water, dried, and crystallized. The diphenyl ester of phenylsulfonamidophosphoric acid gave a yield of 7.02 g (90.2%). The ester is quite soluble in acetone, chloroform, hot alcohol, and difficultly soluble in hot carbon tetrachloride and hot ether. The diphenyl ester is not soluble in water and petroleum ether. It crystallizes very well from benzene and alcohol in the form of transparent, colorless crystals. From carbon tetrachloride it precipitates in the form of long needles with a melting point of 145-146°.

Found %: N 3.49, 3.52. Equivalent (according to phenolphthalein) 0.999, 0.995. $C_{18}H_{16}O_5NSP$. Calculated %: N 3.60. Equivalent 1.00.

For the diphenyl ester of o-tolylsulfonamidophosphoric acid, the yield was 6.65 g (82.5%). It is easily soluble in acetone, chloroform, hot alcohol and benzene, and difficultly soluble in ether; it is insoluble in water. It crystallizes well from alcohol in the form of fine prisms with a melting point of 160-161°.

Found %: N 3.56. Equivalent (according to phenolphthalein) 0.996, 0.997. $C_{19}H_{18}O_5NSP$. Calculated %: N 3.47. Equivalent. 1.00.

The diphenyl ester of α-naphthylsulfonamidophosphoric acid – yield, 7.00 g (79.7%). From dilute alcohol (50%), well formed fine prisms were precipitated with an m. p. of 137-138°. The ester is easily dissolved in acetone, chloroform, dioxane, and alcohol; it is difficultly soluble in hot water.

Found %: N 3.30. Equivalent 1.004, 0.988. $C_{22}H_{18}O_5NSP$. Calculated %: N 3.19. Equivalent 1.00.

The diphenyl ester of β-naphthylsulfonamidophosphoric acid – yield 7.14 g (81.3%). This substance is comparatively quite soluble in hot acetone, chloroform, and benzene and precipitates from these solvents in the form of very fine transparent prisms; it is insoluble in water, ether, petroleum ether and carbon tetrachloride. It crystallizes well from alcohol; m. p. equals 178-179°.

Found %: N 3.27, 3.25. Equivalent (according to phenolphthalein) 0.947, 0.978. $C_{22}H_{18}O_5NSP$. Calculated %: 3.19, Equivalent 1.00.

The hydrolysis of the diphenyl esters of phenyl- and α-naphthylsulfonamidophosphoric acids. 0.003 mole of the diphenyl ester was boiled with 30 ml of a 1 N water-alcohol solution of hydrochloric acid (15 ml of a 2.0 N aqueous solution of hydrochloric acid and 15 ml of alcohol) for 24 hours. After the distilling off of the alcohol in a vacuum over a water bath, an oil was precipitated; the oil quickly began to crystallize. In order to separate the arylsulfamide from the diphenyl ester, the reaction product was washed with water, transferred to a flask and neutralized with a 0.2 N solution of sodium hydroxide until it gave an alkaline reaction to phenolphthalein. Then the mixture was heated and filtered with suction in the hot state. The arylsulfamide remained on the filter; the sodium salt of the diphenyl ester was found in the filtrate. After the cooling of the solution, the sodium salt of the diphenyl ester of α-naphthyl-sulfomanidophosphoric acid was precipitated in the form of very small, lustrous plates.

The arylsulfamides which were separated were identified by the melting point of a mixed sample with the pure amide.

0.16 g (34.0%) of the phenylsulfamide was isolated, m. p. 148-150°; 0.3 g (48.3%) of the α-naphthylsulfamide was separated, m. p. 150-153°.

The preparation of the tricresyl esters of the arylsulfonimidophosphoric acids. In a 100 ml flask was placed 0.03 mole (3.9 g) of dry, finely pulverized o- m- or p-sodium cresolate, and a solution of 0.01 mole of trichlorophosphazosulfonaryl in 20 ml of benzene was added with stirring. The reaction took place energetically with the heating of the mixture, sometimes up to the boiling point of the solvent. The sodium cresolate quickly disappeared and a slimy precipitate of sodium chloride was formed. The reaction mixture was allowed to cool to room temperature and then 30 ml of benzene and 100 ml of a 0.05 N solution of sodium hydroxide was added, after which the mixture was shaken up in a separatory funnel. The benzene extract was washed twice with 100 ml of water

containing sodium chloride, filtered and dried with sodium sulfate. The dry benzene extract, after filtering, was evaporated, and the solvent was driven off in the vacuum of a water-jet pump, over a boiling water bath. In the flask was left the tricresyl ester in the form of a thick oily liquid which had a slight yellow color. In the case of the o-tricresyl ester of phenylsulfonimidophosphoric acid, the oily liquid which was obtained was easily crystallized. The tricresyl esters are quite soluble in acetone, benzene, alcohol and chloroform.

For the o-tricresyl ester of phenylsulfonimidophosphoric acid, the yield was 4.36 g (84.0%). Transparent, colorless needles were obtained (from alcohol); m. p. 90-91°.

Found %: N 2.77. $C_{27}H_{20}O_5NSP$. Calculated %: N 2.76.

The m-tricresyl ester of phenylsulfonimidophosphoric acid gave a yield of 3.7 g (72.9%). The thick transparent liquid, yellow in color, is insoluble in water and petroleum ether.

Found %: N 2.85, 2.80. $C_{27}H_{26}O_5NSP$. Calculated %: N 2.76.

The p-tricresyl ester of phenylsulfonimidophosphoric acid gave a yield of 4.37 g (86.1%). It is a thick, colorless, yellow liquid which is not crystallized on cooling in a freezing mixture.

Found %: N 2.81, 2.77. $C_{27}H_{26}O_5NSP$. Calculated %: N 2.76.

The p-tricresyl ester of o-tolylsulfonimidophosphoric acid gave a yield of 3.2 g (63.1%). The thick, clear, yellow liquid is insoluble in water and petroleum ether. It was not analyzed. It was identified by conversion into the corresponding dicresyl ester (see below).

For the o-tricresyl ester of α-naphthylsulfonimidophosphoric acid, a yield of 3.62 g (65.0%) was obtained. The ester is a very viscous, thick liquid that is yellow in color. It was not analyzed. It was identified by conversion into the corresponding dicresyl ester (see below).

For the p-tricresyl ester of α-naphthylsulfonimidophosphoric acid, the yield was 4.02 g (72.2%). The thick, oily liquid is yellow in color. It was not analyzed. It was identified by conversion into the corresponding dicresyl ester (see below).

The saponification of the tricresyl esters with a water-alcohol solution of sodium hydroxide. 0.002 mole of the full tricresyl ester of the arylsulfonimidophosphoric acid was poured into a 50 ml flask, connected to a reflux condenser; 20 ml of alcohol and 5 ml of a 1.0 N solution of sodium hydroxide was then added. The mixture was heated to boiling for 1 hour, after which the alcohol was distilled off in a vacuum. The precipitate, after the alcohol was driven off, was wholly soluble in water, and therefore, did not contain the tricresyl ester. After the acidification of the aqueous solution with hydrochloric acid (6 ml of a 2.0 N solution), the dicresyl ester was precipitated; it crystallized slowly on being rubbed slightly with a glass rod. The dicresyl ester which is precipitated in the form of an oily layer, is crystallized with considerably more ease if the acidified aqueous solution is decanted with the precipitated oil, and it is well washed with water. The crystalline precipitate is separated, washed, and re-crystallized.

By this method were obtained:

The m-dicresyl ester of o-tolylsulfonamidophosphoric acid, with a yield of 0.52 g (62.4%). It is quite soluble in acetone, chloroform, ether, benzene, hot carbon tetrachloride, and hot alcohol. Well-formed prisms are obtained on crystallization from carbon tetrachloride or dilute alcohol (70%); their m. p. is 107-109°. A mixed sample with the m-dicresyl ester, obtained from m-sodium cresylate and the dichloroanhydride of phenylsulfonamidophosphoric acid, did not give a depression of the melting point.

Found: Equivalent (according to phenolphthalein) 0.97. $C_{20}H_{20}O_5NSP$. Calculated: Equivalent 1.00.

The p-dicresyl ester of o-tolylsulfonamidophosphoric acid, with a yield of 0.68 g (78.8%). The ester is quite soluble in acetone, dioxane, benzene, ether, hot carbon tetrachloride and alcohol. It crystallizes well from carbon tetrachloride and dilute alcohol (70%) in the form of fine, colorless, clear prisms, with a m. p. of 116-117°.

The mixed sample with the p-dicresyl ester, prepared from p-sodium cresylate and the dichloroanhydride of o-tolylsulfonamidophosphoric acid, did not give a depression of the melting point.

Found: Equivalent (according to phenolphthalein) 1.015, 1.016. $C_{21}H_{22}O_5NSP$. Calculated: Equivalent 1.00.

The o-dicresyl ester of α-naphthylsulfonamidophosphoric acid with a yield of 0.76 g (81.3%). The o-dicresyl ester, which is precipitated on the acidification of the alkaline hydrolysis, has the form of a clear, sticky tar, which crystallizes very slowly. On crystallization from alcohol, fine needles with a melting point of 134-136° are obtained.

The ester is quite soluble in acetone, dioxane, ether, and benzene, and is insoluble in carbon tetrachloride and water. It crystallizes well from benzene and alcohol.

Found: Equivalent (according to phenolphthalein) 0.994. $C_{24}H_{22}O_5NSP$. Calculated: Equivalent 1.00.

The yield of p-dicresyl ester of α-naphthylsulfonamidophosphoric acid was 0.78 g (83.4%). After crystallization from alcohol, long needles came down, m.p. 168-169°. A mixed sample with the dicresyl ester prepared from sodium p-cresylate and the dichloroanhydride of α-naphthylsulfonamidophosphoric acid did not give a melting point depression. The ester readily dissolved in acetone, hot benzene, and hot alcohol, and did not dissolve in carbon tetrachloride, ether, or water.

Found: Equivalent (according to phenolphthalein) 1.03. $C_{24}H_{22}O_5NSP$. Calculated: Equivalent 1.00.

The preparation of the dicresyl esters from sodium cresylate and the dichloroanhydrides of the arylsulfonamidophosphoric acids. 20.0 ml of benzene was added with stirring to a mixture of 0.01 mole of finely pulverized dichloroanhydride of the arylsulfonamidophosphoric acid, and 0.03 mole (3.9 g) of sodium cresylate. The reaction took place gently, with little generation of heat (60-70°). The sodium chloride was filtered with suction and the filtrate was evaporated, the solvent being distilled off in a vacuum over a boiling water bath. The residue was dissolved in 100 ml of hot water and the solution was acidified with hydrochloric acid until it gave an acid reaction with a Congo red indicator. The acidified aqueous solution was decanted with the oily precipitate, which was washed with water and allowed to stand until the following day for crystallization. After the dicresyl ester has begun to crystallize, it is washed with water, separated, and dried. For purification it is crystallized from alcohol.

In this way were obtained:

The o-dicresyl ester of phenylsulfonamidophosphoric acid with a yield of 3.51 g (84.0%). The ester is quite soluble in acetone, benzene, hot carbon tetrachloride, and boiling alcohol; the dicresyl ester is insoluble in water and petroleum ether. It crystallizes well from carbon tetrachloride and alcohol (small, fine prisms), the melting point of the crystals being 136-137°.

Found: Equivalent (according to phenolphthalein) 1.023, 1.013. $C_{20}H_{20}O_5NSP$. Calculated: Equivalent 1.00.

The m-dicresyl ester of phenylsulfonamidophosphoric acid, with a yield of 2.95 g (70.6%). After crystallization from alcohol, the crystals melt at 107-109°. The substance is titrated with phenolphthalein as a monobasic acid. A mixed sample with the dicresyl ester obtained by the saponification of the full ester, did not give a lowering of the melting point.

The p-dicresyl ester of phenylsulfonamidophosphoric acid, with a yield of 3.71 g (88.9%). Quite coarse, well-formed, colorless crystals are precipitated from alcohol; their m. p. is 172-173°. Unlike the o- and m-dicresyl esters, the p-dicresyl ester is insoluble in ether and carbon tetrachloride, difficultly soluble in boiling benzene, and is quite soluble in acetone and hot alcohol.

Found: Equivalent (according to phenolphthalein) 0.979, 1.016. $C_{20}H_{20}P_5NSP$. Calculated: Equivalent 1.00.

The p-dicresyl ester of o-tolylsulfonamidophosphoric acid, with a yield of 3.32 g (76.9%). The ester is quite soluble in acetone, benzene, hot carbon tetrachloride, and boiling alcohol, and is insoluble in cold water. It crystallizes well from dilute alcohol (70%) in the form of joined prisms with a m. p. of 116-117°.

Found: Equivalent (according to phenolphthalein) 0.965. $C_{21}H_{22}O_5NSP$. Calculated: Equivalent 1.00.

The p-dicresyl ester of α-naphthylsulfonamidophosphoric acid, with a yield of 3.0 g (64.2%), m. p. 168-169°. The substance was titrated with phenolphthalein as a monobasic acid. A mixed sample with the dicresyl ester, prepared by the saponification of the full ester, did not give a depression of the melting point.

The p-dicresyl ester of β-naphthylsulfonamidophosphoric acid with a yield of 3.81 g (81.5%). It is quite soluble in acetone, hot alcohol and boiling benzene; it is insoluble in ether, water and carbon tetrachloride. It crystallizes well from benzene and alcohol, in the form of fine, small prisms with a melting point of 161-162°

Found: Equivalent (according to phenolphthalein) 0.955, 0.966. $C_{24}H_{22}O_5NSP$. Calculated: Equivalent 1.00.

The preparation of the o-trinitrotriphenyl esters of the arylsulfonimidophosphoric acids. In a round-bottomed flask with a volume of 100 ml connected with a reflux condenser, was placed 0.02 mole of the trichlorophosphazosulfonaryl, 0.06 mole of the finely ground o-sodium nitrophenolate; 30 ml of dry benzene was added. The mixture

was heated for 4 hours on a boiling water bath with constant agitation. After 4 hours of heating there remained a little of the o-nitrophenolate which had not reacted; this did not disappear even on long heating. In the obtaining of the trinitrophenyl ester of the o-naphthylsulfonimidophosphoric acid, the reaction mixture must be heated for not less than 12 hours, since trichlorophosphazosulfonaphthyl reacts with o-sodium nitrophenolate with considerably more difficultl than the trichlorophosphazosulfonphenyl or the o-tolyl. For the separation of the full nitrophenyl esters, 100 ml of benzene was added to the reaction mixture which was then heated and filtered with suction. In the case of α-trichlorophosphazosulfonnaphthyl, it is necessary to use not less than 200 ml of benzene. The benzene extract was then evaporated in a vacuum over a water bath. As the benzene was distilled off, crystals, or more often oily substances which were easily crystallized, were precipitated. The crystalline residue was washed with a small quantity of ether and crystallized from benzene.

In this way we obtained:

The o-trinitrotriphenyl ester of phenylsulfonimidophosphoric acid, with a yield of 9.46 g (78.8%). More than 65 g of the ester was dissolved in 100 ml of boiling benzene. It is insoluble in water, and ether, and is soluble in acetone. On dissolution in alcohol (rectification), it is quickly hydrolyzed. It precipitates from benzene in the form of yellow prisms with a melting point of 94-95°.

Found %: N 9.27, 9.29. $C_{24}H_{17}O_{11}N_4SP$. Calculated %: N 9.33.

The o-trinitrotriphenyl ester of o-tolysulfonimidophosphoric acid with a yield of 9.1 g (74%). More than 13 g and less than 16 g of the ester dissolve in 100 ml of boiling benzene. It is insoluble in water, ether, carbon tetrachloride, and is difficultly soluble in alcohol, and quite soluble in acetone. It precipitates from benzene in the form of coarse, well-formed yellow prisms with a melting point of 151-152°.

Found %: N 8.86, 8.94. $C_{25}H_{19}O_{11}N_4SP$. Calculated %: N 9.11.

The o-trinitrotriphenyl ester of α-naphthylsulfonimidophosphoric acid, with a yield of 6.8 g (52.3%), More than 14 g and less than 20 g was dissolved in 100 ml of boiling benzene. From benzene it is precipitated in the form of fine, clear, yellow prisms with a m. p. of 147-148°. The ester is insoluble in water, ethyl ether, petroleum ether, carbon tetrachloride, and is difficultly soluble in alcohol.

Found %: N 8.41, 8.37. $C_{28}H_{19}O_{11}N_4SP$. Calculated %: N 8.61.

The hydrolysis of the full nitrophenyl esters of the arylsulfonimidophosphoric acids. The preparation of the o-dinitrodiphenyl ester of phenylsulfonamidophosphoric acid. 6.0 g (0.01 mole) of the full o-nitrophenyl ester of phenylsulfonimidophosphoric acid was dissolved in 10 ml of boiling alcohol (rectification) and was allowed to crystallize. Upon a quick crystallization, fine, colorless crystals were precipitated; m. p. equals 150-151°, yield 3.85 g (80.4%). Repeated crystallization from alcohol gave a completely pure substance with a clear m. p. of 150.5-151.0°. Crystallization from benzene did not raise the melting point. The dinitrodiphenyl ester of phenylsulfonamidophosphoric acid is quite soluble in acetone, hot alcohol, and comparatively soluble in hot water; it is insoluble in petroleum ether and carbon tetrachloride, and difficultly soluble in ether and hot benzene.

Found: Equivalent (according to phenolphthalein) 1.03, 1.00. $C_{18}H_{14}O_7N_3SP$. Calculated: Equivalent. 1.00.

The preparation of the o-dinitrodiphenyl esters of o-tolyl- and α-naphthylsulfonamidophosphoric acids. 0.003 mole of the full nitrophenyl ester was dissolved in 10 ml of boiling alcohol. The alcohol was distilled off in a porcelain dish over a water bath. The residue, which was a thick yellow oil, was easily crystallized on the introduction of several drops of water and gentle rubbing with a glass rod. The product was washed several times with ether, in order to wash off the o-nitrophenyl. After washing with ether, the dinitrodiphenyl ester remained in the form of a white powder; it was crystallized from water or dilute alcohol for purification. It is preferable to crystallize larger quantities of the ester from alcohol.

In this way were obtained:

The o-dinitrodiphenyl ester of o-tolylsulfonamidophosphoric acid with a yield of 0.98 g (66.2%). The ester is quite soluble in acetone and hot alcohol and is comparatively soluble in hot water and difficultly soluble in ether and hot benzene. From concentrated aqueous solutions it falls in the form of agregates of small needles, which originate in the one point. From dilute aqueous solutions, clear, well-formed prisms precipitate; their melting point is 131-132°.

Found %: N 7.95. Equivalent (according to phenolphthalein) 0.990, 1.003, $C_{19}H_{16}O_9N_3SP$. Calculated %: N 7.94. Equivalent 1.00.

The o-dinitrodiphenyl ester of α-naphthylsulfonamidophosphoric acid with a yield of 0.95 g (59.9%). It is comparatively easily soluble in hot water and is crystallized from it in the form of well-formed, clear, fine prisms with a m. p. of 172-173°. The ester is quite soluble in hot water and acetone and is insoluble in benzene, carbon tetrachloride, petroleum ether, and is difficultly soluble in ether.

Found: Equivalent (according to phenolphthalein) 1.01, 1.027. $C_{22}H_{16}O_9N_3SP$. Calculated: Equivalent 1.00.

The reactions of the dichloroanhydrides of the arylsulfonamidophosphoric acids with o-sodium nitrophenolates. In a 200 ml flask connected to a reflux condenser was placed 0.02 mole of the dichloroanhydride of the arylsulfonamidophosphoric acid and 0.06 mole of finely ground o-sodium nitrophenolate; 100 ml of benzene was added. The mixture was heated on the boiling water bath until the main part of the sodium nitrophenolate had reacted; this took about 20 hours. For the separation of the dinitrodiphenyl esters, the reaction mixture was evaporated, the benzene being distilled off in vacuum over a water bath. 200 ml of water was added to the residue, well mixed, and allowed to stand. The aqueous solution was decanted with the oily layer of the nitrophenol and acidified with hydrochloric acid until it gave an acid reaction with Congo red. The dinitrodiphenyl ester was precipitated from the acidified solution in the form of yellow, oily layer, which gradually crystallized. The crystalline precipitate was well washed with water and filtered with suction.

In this way were obtained:

The o-dinitrodiphenyl ester of phenylsulfonamidophosphoric acid, with a yield of 8.43 g (70.3%). After crystallization from alcohol or from water, the melting point was 150-151°. A mixed sample with the dinitrodiphenyl ester, prepared by the hydrolysis of the full nitrophenyl ester, did not give a depression of the melting point.

Found: Equivalent (according to phenolphthalein) 1.005. $C_{18}H_{14}O_9N_3SP$. Calculated: Equivalent 1.00.

The o-Dinitrodiphenyl ester of o-tolylsulfonamidophosphoric acid, with a yield of 3.40 g (34.5%). After crystallization from water, the melting point was 161-162°. A mixed sample with the dinitrodiphenyl ester, prepared by the hydrolysis of the full nitrophenyl ester, melted at the same temperature. The substance was titrated with phenolphthalein as a monobasic acid.

SUMMARY

1. The reactions of the trichlorophosphazosulfonaryls with sodium phenolate, sodium cresylates, and with o-nitrophenolate have been studied.

2. The full aromatic esters of the arylsulfonimidophosphoric acids have been prepared, and their properties have been described.

3. The hydrolysis of the full aromatic esters of the arylsulfonimidophosphoric acids has been studied.

4. The diaryl esters of the arylsulfonamidophosphoric acids have been prepared and their properties have been described.

5. We have prepared and described the o-trinitrotriphenyl esters of the arylsulfonimidophosphoric acids and the o-dinitrodiphenyl esters of the arylsulfonamidophosphoric acids, and have described their properties.

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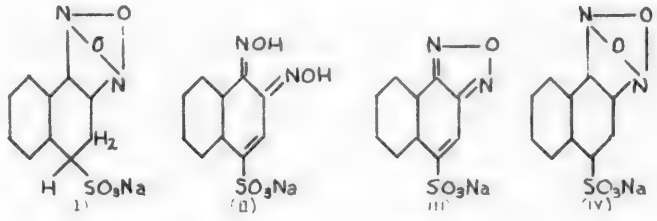
STUDIES IN THE NAPHTHOFUROXANE SERIES

III. 1,2-NAPHTHOQUINONEDIOXIME-4-SULFONIC ACID

S. V. Bogdanov and I. N. Koroleva

As has already been pointed out [1], the bisulfite compounds of naphthofuroxane (I) on the action of soda, (depending on the conditions) are converted into 2-nitro-1-naphthylamine-4-sulfonic acid, or into 2-nitro-1-naphthol-4-sulfonic acid; the following products are also obtained in small quantities: naphthofuroxane, naphthofurazan, and a sulfonic acid of unknown structure. The process takes place differently when the soda is replaced by sodium hydroxide. In this case, when the reaction is carried out at first with cooling, and then at ordinary temperature, with the use of 5 moles of the alkali to one mole of the bisulfite compound, the main product (with yields up to 75%) is 1,2-naphthoquinonedioxime-4-sulfonic acid (II). In addition, 1,2-naphtho-(3',4')-furazan-4-sulfonic acid (III) is obtained, and small quantities of naphthofuroxane and naphthofurazan. On the heating of the bisulfite compounds with a solution of sodium hydroxide, naphthofurazan-4-sulfonic acid is formed, and, in considerably smaller quantities, 2-nitro-1-naphthol-4-sulfonic acid. The above-mentioned sulfonic acid, which was obtained as a by-product in a soda solution, also turned out to be naphthofurazan-4-sulfonic acid. Naphthofurazan-4-sulfonic acid is a product of the further conversion of 1,2-naphthoquinonedioxime-4-sulfonic acid, and is easily obtained on the treatment of the latter with sodium hydroxide or with acetic anhydride. Earlier [2] it was separated from the products of the reaction of 1-nitroso-2-naphthol-4-sulfonic acid with hydroxylamine in an alkaline solution. The formation of naphthofurazan-4-sulfonic acid in a soda solution and 2-nitro-1-naphthol-4-sulfonic acid in a sodium hydroxide solution shows that in both cases the decomposition of the furoxane ring goes in two directions. One of these leads to 2-nitro-1-naphthylamine-4-sulfonic acid, and the other to 1,2-naphthoquinonedioxime-4-sulfonic acid. The degree of basicity of the solution determines only the main path of the reaction.



1,2-Naphthoquinonedioxime-4-sulfonic acid, on the action of weak hydrochloric acid, is converted into 2-nitro-1-naphthol-4-sulfonic acid, and on reduction with stannous chloride, is converted into 1,2-naphthalenediamine-4-sulfonic acid; on oxidation with nitric acid it converts into naphthofuroxane-4-sulfonic acid (IV).

Naphthofuroxane-4-sulfonic acid, on reduction with zinc (preferably in the presence of a small amount of stannous chloride) is converted into 1,2-naphthalenediamine-4-sulfonic acid, and on the action of potassium hypochlorite and hydrochloric acid it is converted into 4-chloronaphthofuroxane.

EXPERIMENTAL

1,2-Naphthoquinonedioxime-4-sulfonic acid. 28.6 ml (0.5 mole) of 46% sodium hydroxide was added to a suspension of 34.4 g (0.1 mole) of the sodium salt of the bisulfite compound of naphthofuroxane in 175 ml of water, the suspension being first cooled to 5°. The mixture was kept at 5° for two hours, and then at 18-20° for 18 hours. The turbid red-orange solution was filtered, and the residue was washed with water (residue "a"; 0.4 g). 45 ml of 35.4% hydrochloric acid, diluted with 100 ml of water, was gradually added to the filtrate at a temperature of 5-10°. Upon acidification, the evolution of sulfur dioxide gas was detected The suspension of the sodium salt of naphthoquinonedioxime-sulfonic acid which was formed was cooled at 0°, the residue was filtered and washed with water and methyl alcohol; the yield was 24.87-25.8 g, i.e., 72.3-75.0%.

The filtrate, after the addition of sodium acetate, was concentrated by evaporation to a small volume, and the residue which was precipitated was filtered (residue "b").

On the shortening of the length of the experiment to 3 hours and 0.5 hours, the yield fell to 62.5 and 55.7% respectively, and on decreasing the quantity of sodium hydroxide to 2 moles and 1 mole per mole of the bisulfite compound (with the original length of time of the experiment) the yield fell to 51.2 and 46.8%.

On the crystallization of residue ("a") from alcohol naphthofuroxane (m. p. equals 124-125.5°) and naphthofurazan (m. p. 76-78°) were obtained.

On the recrystallization of residue("b")from water a substance with the properties of naphthofurazan-4-sulfonic acid was obtained (see below). The sulfochloride has a m. p. of 112.5-113.5°.

The sodium salt of naphthoquinonedioximesulfonic acid is quite soluble in water, and more difficultly soluble in alcohol; it is very easily soluble in alkalis, forming an orange solution. Aqueous solutions are colored by iron vitriol to a deep, turbid violet color. In the presence of admixtures of 2-nitroso-1-naphthol-4-sulfonic acid (which is obtained with uncareful separation of the reaction product with hydrochloric acid) a green coloration appears in the first moment after the addition of the iron vitriol; this quickly changes to violet. It crystallizes in the form of long yellow prisms (from water). It contains 3 molecules of water of crystallization, which is not driven off at 100-110°; the substance decomposes at 120-130°.

6.900 mg sub.: 8.800 mg CO_2; 2.380 mg H_2O. 3.916 mg sub.: 0.284 ml N_2 (24°, 732 mm). 0.1050 g sub.: 0.0214 g Na_2SO_4. Found %: C 34.80; H 3.86; N 8.03; Na 6.60. $C_{10}H_7O_5N_2SNa \cdot 3H_2O$. Calculated %: C 34.87; H 3.80; N 8.14; Na 6.68.

The potassium salt is somewhat less soluble in water than the sodium salt. It crystallizes in the form of orange-yellow prisms. It has 1 molecule of water of crystallization, and responds to heating in the same way as the sodium salt.

5.248 mg sub.: 7.204 mg CO_2; 1.234 mg H_2O. 3.697 mg sub.: 0.279 ml N_2 (21°, 745 mm). 0.2203 g sub.: 0.1611 g $BaSO_4$; 0.2362 g sub.: 0.0630 g K_2SO_4. Found %: C 37.44; H 2.63; N 8.59; S 10.04; K 11.97. $C_{10}H_7O_5N_2SK \cdot H_2O$. Calculated %: C 37.03; H 2.80; N 8.64; S 9.89; K 12.06.

The silver salt crystallizes in the form of curved, yellow needles. It is slightly soluble in cold water and decomposes in hot water.

0.4386 g sub.: 11.49 ml 0.1 N NH_4CNS. Found %: Ag 28.26. $C_{10}H_7O_5N_2SAg$. Calculated %: Ag 28.77.

The benzidine salt crystallizes in the form of yellow cubic prisms. It is slightly soluble in water and is decomposed in hot water.

1.8468 g sub.: 49.35 ml 0.1 N $NaNO_2$. Found: M 748.5. $C_{32}H_{28}O_{10}N_6S_2 \cdot 2H_2O$. Calculated: M 756.7.

2-Nitroso-1-naphthol-4-sulfonic acid. A solution of 34.4 g of the sodium salt of naphthoquinonedioximesulfonic acid in 300 ml of water was acidified with 9 ml of 35.4% hydrochloric acid and boiled for 2 hours. The sodium salt of nitrosonaphtholsulfonic acid, which was precipitated, was filtered and washed with water; the yield was 23.0 g (75%). It crystallizes in the form of yellow needles from water. This substance gives an intense green color with iron vitriol. On heating with zinc in the presence of traces of acetic acid, a colorless solution which quickly changes to a blue coloration is formed; on acidification the color becomes red, and on alkalization it becomes green. On reduction with stannous chloride 2-amino-1-naphthol-4-sulfonic acid is formed, and on oxidation with nitric acid 2,4-dinitro-1-naphthol is formed; m. p. 138.5 (decomposes).

1.1162 g sub.: loss on desiccation (120°) 0.1100 g. 0.2788 grams of the dry substance : 0.0704 g Na_2SO_4. Found %: H_2O 9.86; Na 8.18. $C_{10}H_6O_5NSNa \cdot 1.75\ H_2O$. Calculated %: H_2O 10.23. $C_{10}H_6O_5NSNa$. Calculated %: Na 8.36.

1,2-Naphtho-(3',4')-furazan-4-sulfonic acid. 1) A solution of 6.55 g of 98% sodium hydroxide in 18 ml of water was added to a suspension of 13.77 g of the sodium salt of 1,2-naphthoquinonedioxime-4-sulfonic acid in 40 ml of water; the obtained solution was held for 1 hour at 15°, and then boiled for 15 minutes. After cooling, the sodium salt of naphthofurazansulfonic acid which was precipitated was filtered and washed with water and alcohol: the yield was 9.8 g (87%).

The sodium salt was quite soluble in water and was crystallized in the form of long colorless prisms. It contains 1/2 of a molecule of water of crystallization, which is not driven off at 160°.

5.430 mg sub.: 8.538 mg CO_2; 0.910 mg H_2O. 4.234 mg sub.: 0.365 ml N_2 (21°, 736 mm). 0.2268 g sub.: 0.0560 g Na_2SO_4. Found %: C 42.89; H 1.88; N 9.69; Na 8.00. $C_{10}H_5O_4N_2SNa \cdot 0.5H_2O$. Calculated %: C 42.71; H 2.15; N 9.96; Na 8.18.

The aniline salt is difficultly soluble in water and is crystallized in the form of thin colorless plates; m. p. is 277° (decomposes).

0.3684 g sub.: 10.74 ml 0.1 N $NaNO_2$. Found: M 343. $C_{16}H_{13}O_4N_3S$. Calculated: M 343.

The sulfochloride crystallizes in the form of cubic prisms (from benzene); m. p. 112.5-113.5°.

2) A suspension of 3 g of the sodium salt of naphthoquinonedioximesulfonic acid in 90 ml of acetic anhydride was boiled for 12 hours; the residue gradually grew lighter. The sodium salt of naphthofurazansulfonic acid which was precipitated was filtered and washed with water and methyl alcohol; the yield was 3.6 g. The m. p. found for the sulfochloride was 112.3-113.5.

3) 8.6 g ml of 46.7% sodium hydroxide was added to a solution of 10.33 g of the sodium salt of the bisulfite compound of naphthofuroxane in 75 mm of water at 30°, and the mixture was boiled for 2 hours. The reaction product began to precipitate after only 10 minutes of boiling. After the cooling of the mixture, the residue of the sodium salt of naphthofurazansulfonic acid was filtered and washed with water and methyl alcohol; the yield was 5.17 g. Fractional evaporation of the filtrate separated 1.82 g more of the substance. The m. p. of the sulfochloride was 112.5-113.5°

The filtrate from the sodium salt of naphthofurazansulfonic acid, after the addition of water, was acidified with hydrochloric acid, and the residue of the sodium salt of 2-nitro-1-naphthol-4-sulfonic acid, which was precipitated, was then filtered; the yield was 0.73 g.

It crystallizes in the form of thin yellow plates (from water). The substance did not give reaction for 2-nitroso-1-naphthol-4-sulfonic acid, and on heating with nitric acid was converted into 2,4-dinitro-1-naphthol; on reduction with stannous chloride it converted into 2-amino-1-naphthol-4-sulfonic acid

The by-product which was formed by the action of soda on the bisulfite compound was crystallized from water in the form of long, colorless, prisms, and contained 7.99% sodium.

The m. p. of the sulfochloride was 112.8-113.5°.

1,2-Naphthofuroxane-4-sulfonic acid. 52 ml of 55.8% nitric acid was added to a suspension of 20.0 g of the sodium salt of 1,2-naphthoquinonedioxime-4-sulfonic acid in 100 ml of water at 20°; the mixture was held for 1 hour at 90° and for 15 minutes at 100°. After cooling the sodium salt of naphthofuroxanesulfonic acid was filtered, and washed with water and methyl alcohol; the yield was 14.0 g. On the neutralization of the filtrate with soda, 1.2 g more of the substance was separated. The total yield was 90.8%.

The sodium salt is difficultly soluble in water and is crystallized in the form of short colorless prisms; it does not contain water of crystallization.

6.312 mg sub.: 9.586 mg CO_2; 1.030 mg H_2O. 3.539 mg sub.: 0.311 ml N_2 (26°, 744 mm). 0.1900 g sub.: 0.0468 g Na_2SO_4. Found %: C 41.45; H 1.83; N 9.82; Na 7.97. $C_{10}H_5O_5N_2SNa$. Calculated %: C 41.67; H 1.75; N 9.72; Na 7.98.

1,2-Naphthalenediamine-4-sulfonic acid. 1) A solution of 18 g of crystalline 95% stannous chloride in 30 ml of 35.4% hydrochloric acid and 20 ml of water, was added to a solution of 5.18 g of the sodium salt of naphthoquinonedioximesulfonic acid in 50 ml of water, at 45°. The liquid, which becomes a yellow-brown color, was boiled for 10 minutes. On cooling, the residue of 1,2-naphthalenediamine-4-sulfonic acid was filtered; the yield after reprecipitation from a sodium acetate solution was 2.77 g. It crystallizes in the form of long prisms. With a bisulfite compound of phenanthrenequinone, it gives naphthophenanthrazinesulfonic acid (yellow needles), and on oxidation with nitric acid, it gives 1,2-naphthoquinone-4-sulfonic acid.

The sulfochloride of naphthoselenoidiazolesulfonic acid was prepared in the way that has been described previously [3]. It crystallized in the form of bipyramides (from chlorobenzene), m. p. 205-206°.

2) 0.5 g of crystalline stannous chloride was added to a solution of 2 g of the sodium salt of naphthofuroxanesulfonic acid in 150 ml of water at 80° after the latter solution had been acidified with 15 ml of 35.4% hydrochloric acid; 5.2 g of zinc powder was then added over the course of 25 minutes. The strongly frothing mass was stirred at 80° for 30 minutes and then cooled. The napththalenediaminesulfonic acid which was formed was filtered and

reprecipitated from a solution of sodium acetate; the yield was 1.47 g. On reduction with zinc in the absence of stannous chloride, the yield fell to 0.67 g.

The sulfochloride of naphthoselenodiazolesulfonic acid: m. p. 205-206°.

4-Chloro-1,2-naphthofuroxane. A solution of 2.94 g of potassium chlorate in 50 ml of water was added with stirring over the course of an hour to a boiling solution of 5.76 g of the sodium salt of 1,2-naphthofuroxane-4-sulfonic acid in 320 ml of water, which had been acidified with 11.2 ml of 35.5% hydrochloric acid. The reaction mixture was mixed while boiling for 1 hour, cooled, and the product of chlorination which was precipitated was filtered; the yield was 3.38 g, m. p. was 124-130°. The substance is quite soluble in acetic acid and alcohol, and crystallizes from alcohol in the form of curved needles which melt at 140.2-140.8°.

5.260 mg sub.: 10.520 mg CO_2; 1.136 mg H_2O; 0.852 mg Cl. 3.694 mg sub.: 0.402 ml N_2 (22°, 736 mm). Found %: C 54.56; H 2.42; Cl 16.19; N 12.20. $C_{10}H_5O_2N_2Cl$. Calculated %: C 54.44; H 2.28; Cl 16.07; N 12.71.

SUMMARY

1. The main product of the decomposition of the bisulfite compounds of naphthofuroxane by sodium hydroxide, first with cooling and then at room temperature, is 1,2-naphthoquinonedioxime-4-sulfonic acid. Naphthofuroxane, naphthofurazan and naphthofurazan-4-sulfonic acid are formed as by-products.

2. On the decomposition of the bisulfite compound by sodium hydroxide with heating naphthofurazan-4-sulfonic acid and a small amount of 2-nitro-1-naphthol-4-sulfonic acid are obtained.

3. 1,2-Naphthoquinonedioxime-4-sulfonic acid, on the action of hydrochloric acid is converted into 2-nitroso-1-naphthol-4-sulfonic acid, and on treatment with sodium hydroxide or acetic anhydride is converted into naphthofurazan-4-sulfonic acid; on reduction it is converted into 1,2-naphthalenediamine-4-sulfonic acid, and on oxidation with nitric acid into naphthofuroxane-4-sulfonic acid.

4. Naphthofuroxane-4-sulfonic acid, on the action of potassium chlorate and hydrochloric acid is converted into 4-chloronaphthofuroxane.

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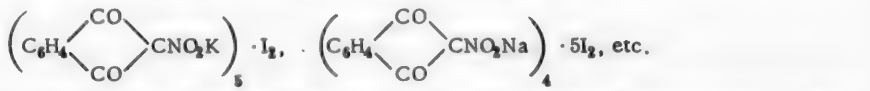
* T. p. = C. B. Translation pagination.

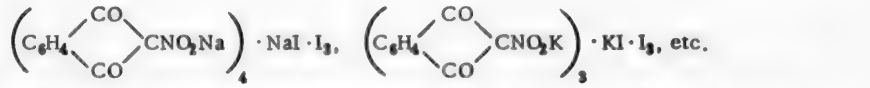
COMPLEX SALTS OF N-HYDROXYPHTHALONIMIDE WITH POLYIODIDES

E. Vanag and G. Vanag

2-Nitro-1,3-indandione (I) is a pseudo hydrogen halide acid and its salts give crystalline complex salts with iodine [1, 2]. These compounds are not formed very easily and they lose iodine when exposed to the air. For example, depending on the preparation conditions, the following compounds were obtained:

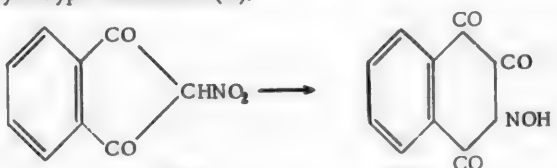


The ternary complexes are the most easily formed, i.e. those compounds in which the corresponding iodide is still retained, for example:



These complexes also lose part of their iodine when exposed to the air. All of these complex salts are dark-colored crystalline substances with a bronze reflex.

It was recently shown by us [3, 4] that nitroindandione, under the influence of acid anhydrides and some other substances, is isomerized to N-hydroxyphthalonimide (II):

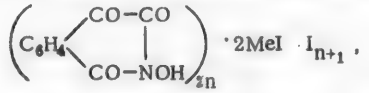


(I) (II)

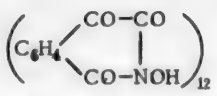
The latter already fails to show the properties of a pseudo hydrogen halide acid; consequently, it was of interest to determine if the ability to form complexes with polyiodides was still retained. It was found that N-hydroxyphthalonimide is also very prone to such complex formation and that the resulting complexes are more stable than are the complex salts of the nitroindandione.

Fialkov and coworkers [5-10] have made a systematic study of the polyhalide type of complexes and come to the conclusion that compounds of a definite composition are frequently formed. Godina and Faerman [11], in studying the complexes of quinine sulfate with iodine, of which 7 are described in the literature, came to the conclusion that stoichiometrically determined ratios fail to exist between the amounts of iodine and hydroiodic acid, and that the amount of iodine entering into the composition of the polyhalide compounds is variable depends on the amount of excess iodine present at the time the compound is formed, and fails to obey stoichiometric rules. In all cases "adsorbed polyiodides" are formed, failing to represent stoichiometrically determined compounds.

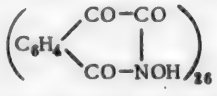
As already mentioned, the salts of nitroindandione with iodine and polyiodides also have a variable composition depending on the preparation conditions. The composition of the complex salts of N-hydroxyphthalonimide proved to be independent of the amount of iodine in solution. In addition, it was found possible to depict the composition of many of the complex salts of N-hydroxyphthalonimide with metal polyiodides by the general formula:



where: n – is a whole number, and Me – is a univalent cation. Thus, for example, the complex potassium salt has the composition:



where n, consequently, is equal to 6. The sodium and ammonium salts also have a similar composition. These salts are stable and fail to lose iodine when allowed to stand in the air. The freshly prepared complex salts of barium, strontium, calcium and nickel also correspond to the general formula, but on standing in the air they lose 1 atom of iodine. The ethylenediamine salt also corresponds to the general formula, where n = 13:



This salt fails to change when allowed to stand in air.

The complex salts are obtained as follows: N-hydroxyphthalonimide is treated with a solution of iodine in the corresponding iodide and the mixture heated. The N-hydroxyphthalonimide goes into solution, and from the solution on cooling the complex salt precipitates as dark-colored crystals with a metallic luster. The complex salts can be recrystallized from water, but in quite low yields, since the salt suffers partial decomposition when heated with water.

Having determined the total amount of iodine in the compound and the ratio of "free" iodine to iodide ion (I : I'), and knowing that the complex (compound) fails to contain any components other than N-hydroxyphthalonimide, metal iodide and "free" iodine, it then becomes possible on the basis of these data to calculate the composition of the complex. The validity of the obtained formula is then confirmed by determining the nitrogen (from the N-hydroxyphthalonimide) and the corresponding metal.

The salts were analyzed by the method developed by us for the analysis of the complex salts of nitroindandione [1, 2]. The active ("free") iodide was determined by titration with thiosulfate, the iodide ion by the Fajens titration method, and nitrogen by the micro Dumas method, and the corresponding cation by the general methods for the determination of metals in organic compounds. The results are given in the Table.

Complex Salts of N-Hydroxyphthalonimide With Polyiodides

Expt. No.	Salt composition		I (in %)			N in %	Cation in %	Condition of salt when Analyzed
			Total	"Free"	ion			
1	$(Nfi)_{12} \cdot 2NaI \cdot I_7$	Found	34.10	26.23	7.87	4.85	1.41	
		Calculated	32.83	25.54	7.30	4.83	1.32	
2	$(Nfi)_{12} \cdot 2KI \cdot I_7$	Found	33.49	25.91	7.58	4.71	2.30	
		Calculated	32.53	25.30	7.23	4.78	2.26	
3	$(Nfi)_{12} \cdot 2NH_4I \cdot I_7$	Found	33.79	25.79	8.00	5.52		
		Calculated	32.94	25.62	7.32	5.65		
4	$(Nfi)_{12} \cdot CaI_2 \cdot I_7$	Found	32.84	25.65	7.19	5.18		Fresh
		Calculated	32.90	25.59	7.31	4.83		
5	$(Nfi)_{10} \cdot SrI_2 \cdot I_5$	Found	30.71	22.30	8.35	5.40	2.34	
		Calculated	30.79	22.00	8.80	4.85	3.05	Aged
6	$(Nfi)_{12} \cdot BaI_2 \cdot I_7$	Found	31.24	24.24	7.00	4.91	3.75	
		Calculated	32.00	24.89	7.11	4.70	3.83	Fresh
7a	$(Nfi)_{12} \cdot NiI_2 \cdot I_7$	Found	32.38	25.14	7.14			
		Calculated	32.71	25.45	7.27			Fresh
7b	$(Nfi)_{12} \cdot NiI_2 \cdot I_6$	Found	29.82	22.57	7.25	5.28	1.64	
		Calculated	30.17	22.63	7.54	4.99	1.75	Aged
8	$(Nfi)_{10} \cdot ZnI_2 \cdot I_4$	Found	27.42	18.54	8.88	5.19		
		Calculated	27.84	18.57	9.30	5.11		Aged
9	$(Nfi)_{26} \cdot En \cdot 2HI \cdot I_{14}$	Found	28.00	24.51	3.48	5.53		
		Calculated	28.78	25.19	3.60	5.55		

Remarks: Nfi – N-hydroxyphthalonimide; En – ethylenediamine; fresh – freshly prepared; aged – allowed to stand in the air to constant weight.

As can be seen, the complex salts of N-hydroxyphthalonimide with polyiodides have a very complex composition. They can be classified as belonging to the group of multinuclear or "ultracomplex" compounds [12]. A closer study of their structure was not made. Purely schematically, for example, the potassium salt can be depicted as follows (Nfi = N-hydroxyphthalonimide):

EXPERIMENTAL

Potassium Salt. The N-hydroxyphthalonimide (0.5 g) is treated with several milliliters of a potassium iodide solution of iodine and the mixture heated until the N-hydroxyphthalonimide is completely dissolved and a transparent dark-brown solution is formed. On cooling, a precipitate of dark-colored plates with a metallic luster is obtained, uniformly permeating all of the liquid. The cooled mixture is suction filtered, washed with cold water, and dried at room temperature. The dry salt is removed from the filter paper as dark-colored pliant platelets. Yield 0.4 g. Its solubility in cold water is approximately 1 g per liter; the solution is brown-colored, and with starch it gives a blue coloration. It fails to give a precipitate with the ions of barium, strontium, calcium, nickel or copper; with silver and lead ions the precipitates of the corresponding iodides are obtained.

Sodium and Ammonium Salts. Obtained in the same manner as the potassium salt and fully comparable to it in their properties.

Barium Salt. Prepared the same as the potassium salt. Dark-colored crystals with a metallic reflex. On standing in the air for 3 weeks the salt lost 1 atom of iodine.

Strontium Salt. Prepared the same as the potassium salt. In external appearance it differs from the preceding salts; it fails to have the characteristic surface luster. On standing in the air the salt gradually loses iodine, for example, after 3 days the weight loss was 1%. To determine exactly the amount of iodine lost the salt was first dried in a desiccator over sulfuric acid in iodine vapors (an iodine crystal was placed in the desiccator), after which it was left in the open air. A month was required for the salt to establish a constant weight. The total weight loss was 2.93%; for the loss of 1 atom of iodine the theoretical weight loss should have been 3.28%.

Calcium Salt. Depending on the conditions variable precipitates were obtained – some as gels and others in the crystalline form. The composition of the freshly prepared crystalline salt corresponds to the general formula, while the gel, after its constant weight had been established, corresponds to the formula:

$$(Nfi)_{10} \cdot CaI_2 \cdot I_4.$$

Nickel Salt. Prepared the same as the potassium salt. A crystalline precipitate with a greenish reflex. After 3 weeks in the air it loses 1 atom of iodine.

Zinc Salt. Prepared the same as the potassium salt. The yields were low. The crystals were not as well-formed as for the salts of the alkali metals, neither was the charactersitic surface luster present. In the air the salt loses iodine. In accord with the general formula the salt is minus 2 atoms of iodine. Due to the low yields the salt was not studied closer.

Ethylenediamine Salt. The ethylenediamine was dissolved in an equivalent amount of hydroiodic acid, the iodine was dissolved in the iodide solution thus obtained, and the N-hydroxyphthalonimide was treated in the usual manner with this solution. Dark-colored crystals were obtained, reminiscent of the complex salts of the alkali metals. The composition of the salt corresponds to the general formula.

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BORON FLUORIDE AS A CATALYST IN ORGANIC CHEMISTRY

X. ALKYLATION OF ANISOLE WITH PSEUDOBUTYLENE

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The alkylation of phenols with olefins in the presence of boron fluoride and its molecular compounds has been studied by a number of investigators. In our laboratory a study was made of the alkylation of phenols and the chlorophenols with pseudobutylene and 2-pentene in the presence of the boron fluoride-ethyl ether complex [1-3]. There are no original investigations on the alkylation of alkylphenyl ethers with olefins in the presence of boron trifluoride, and only a few patent communications exist. To accomplish this task we have made in recent years some systematic studies of the reaction between the alkylphenyl ethers and unsaturated compounds. In the present paper we describe the results obtained for the alkylation of anisole with pseudobutylene in the presence of $BF_3 \cdot O(C_2H_5)_2$, $BF_3 \cdot H_3PO_4$ and BF_3 with reactant ratios of 1:1, 1:2 and 1:2.5, and temperatures ranging from −5 to 100°.

As our studies revealed, the boron fluoride-ethyl ether complex, possessing high activity for the alkylation of phenol with pseudobutylene [1], proved to be but slightly effective for the above indicated reaction. Thus, anisole and pseudobutylene in the presence of 9% of $BF_3 \cdot O(C_2H_5)_2$, heated on the boiling water bath for 4 hours, give sec-butylanisoles in 24% of the theoretical yield. The extent of alkylation is almost nil when the amount of catalyst is reduced to 4%.

The compound of boron fluoride with orthophosphoric acid shows a higher catalytic activity. For example, if the reaction of gaseous pseudobutylene with anisole is carried out at room temperature in the presence of BF_3-saturated orthophosphoric acid, the sec-butylanisoles are obtained in 40% of the theoretical yield. Almost the same yield (37%) of alkylate is obtained if liquid pseudobutylene, anisole, and BF_3-saturated orthophosphoric acid are mixed at one time and the reaction mixture shaken for 8 hours at room temperature. Elevation of the temperature to 50 and 90°, but with the ratios of reactants and catalyst kept constant, increases the absorption rate of the pseudobutylene by the anisole and catalyst, the degree of alkylation is raised, and the sec-butylanisoles are obtained in 56% yield at 40-50° and a 66% yield at 80-90°.

Variation in the molar ratios of anisole to pseudobutylene from 1:1 to 1:2 and 1:2.5 also exerts a favorable influence on the reaction and gives a higher yield of alkylate for corresponding conditions.

Variation in the amount of BF_3 catalyst within the limits of 9 to 17% has very little effect on the degree of alkylation. However, a certain minimum exists for the boron fluoride, below which the degree of alkylation is greatly reduced. For example, a reduction in the amount of boron fluoride from 12 to 6% retards the absorption rate of the pseudobutylene by the anisole and $BF_3 \cdot H_3PO_4$ and reduces the yield of alkylate more than 2-fold (from 56 to 25%).

In contrast to the alkylation of aromatic hydrocarbons with olefins in the presence of $BF_3 \cdot H_3PO_4$, in the present reaction this catalyst and alkylate mix well and fail to separate on standing; for this reason the catalyst can only be used once.

When the alkylation of anisole with pseudobutylene is carried out in the presence of BF_3 alone, without the orthophosphoric acid, the absorption of pseudobutylene under comparable conditions (ratio of reactants 1:1, 16% of BF_3, and room temperature) is even better than in the presence of orthophosphoric acid, and the sec-butylanisoles are obtained in the same yield as when $BF_3 \cdot H_3PO_4$, is used. The use of larger amounts of BF_3, of the order of 25% to the total amount of reactants, gives an 82% yield of the alkylate, based on anisole. But under these conditions the alkylation is more profound and the exothermic heat developed during the time of pseudobutylene introduction raises the temperature of the reaction mixture to 60°. As a result the mono- and di-sec-butylanisoles are obtained in approximately equal amounts. Consequently, anhydrous orthophosphoric acid fails to exert any influence on the catalytic activity of boron fluoride in the given reaction, and for this reason the need to use it no longer exists. The use of boron fluoride without the phosphoric acid facilitates the isolation of the alkylation products, since on treating the reaction products with alkali an emulsion that separates into layers only after long standing is no longer formed. But the chief advantage here is the fact that up to 70% of the boron fluoride taken for reaction can be recovered by simple heating of the reaction mixture (prior to the alkali treatment) to 130-140°.

On the basis of the isolated products it can be concluded that in the alkylation of anisole with pseudobutylene in the pressure of 6-18% of BF_3 and its molecular compounds with H_3PO_4 and $O(C_2H_5)_2$ at temperatures of −5 to 100° a mixture of mono-sec-butylanisoles is mainly formed (75%), of which the chief component is o-sec-butylanisole. As a result, the alkylation proceeds first of all in the ortho-position.

EXPERIMENTAL

Reagents. The anisole used was the commercial freshly-distilled product with b. p. 150-152°, d_4^{17} 0.9972, n_D^{17} 1.5165. The pseudobutylene was isolated from a pseudobutylene-bivinyl (1,3-butadiene) fraction containing 60-80% of pseudobutylene.

Catalysts. The boron fluoride was obtained from CaF_2, B_2O_3 and concentrated H_2SO_4. The molecular compound of boron fluoride with orthophosphoric acid was obtained by saturating anhydrous orthophosphoric acid with boron fluoride until the weight increase corresponded to that of the compound $BF_3 \cdot H_3PO_4$; the substance was a clear, yellowish, viscous liquid and was used without previous distillation due to its ease of decomposition. The ethyl ether complex of boron fluoride was obtained by the passage of BF_3 into anhydrous ethyl ether, and after distilling off the excess ether, distilled at 124-127° as a colorless liquid that fumed easily in the air; it was used freshly distilled.

The alkylation of anisole with gaseous pseudobutylene in the presence of $BF_3 \cdot H_3PO_4$ and BF_3 catalyst was run as follows: a weighed amount of anhydrous orthophosphoric acid was placed in a three-necked flask and to it was added BF_3 until the weight increase approximately corresponded to that of the compound $BF_3 \cdot H_3PO_4$. Anisole was then added to the prepared catalyst. In the reaction with BF_3 alone the anisole was first placed in the flask and then saturated with boron fluoride. The flask through its central opening was connected to a mechanical stirrer and was fitted with a mercury seal and reflux condenser, the latter being connected to a gasometer for collecting unreacted pseudobutylene. A thermometer was inserted in one of the side openings, and through the second opening, by means of a gas inlet tube reaching to the bottom of the reaction flask, a flask, filled with pseudobutylene and supplied with a stopcock, was connected. Then, with vigorous stirring, the pseudobutylene was passed into the anisole-catalyst mixture at a rate of 1.8 to 4.7 liters/hr., depending on the absorption intensity. At room temperature the pseudobutylene absorption was comparatively slight at the start, but after a certain induction period (in approximately 30-40 minutes after the start of pseudobutylene addition) the absorption rate rose sharply, and heating up of the reaction mixture was observed.

After adding a definite amount of pseudobutylene the stirring of the mixture was continued for another 2-6 hours. The alkylate and catalyst as a homogeneous liquid, of yellow color in the case of reaction at room temperature, and reddish-brown in the case of reaction at elevated temperature, was allowed to stand overnight at room temperature, after which it was diluted with a small amount of water (in the experiments with $BF_3 \cdot H_3PO_4$), the alkylate separated, treated with 5% soda solution, washed with water, dried over calcium chloride, and distilled. The unreacted anisole was removed by distillation at atmospheric pressure to 165°, while the residue was vacuum-distilled. The alkylate distilled almost completely. The residue from 15-40 g of alkylate subjected to fractionation was 0.2-2.0 g of heavy dark-brown oil. Such an oil from one of the experiments had d_4^{20} 1.010, n_D^{20} 1.5357. The fractions were collected in a boiling range of 25-30°. They were colorless oily liquids with a pleasant odor. In the experiments with BF_3 the reaction mixture, prior to neutralization with soda solution, was heated to 130-140°. The boron fluoride evolved here was passed into anhydrous ethyl ether. Then the alkylation products were treated as described above.

For the alkylation of anisole with liquid pseudobutylene in the presence of either $BF_3 \cdot O(C_2H_5)_2$ or $BF_3 \cdot H_3PO_4$ the anisole was placed in a wide test tube and the boron fluoride-ethyl ether complex was added, or anhydrous orthophosphoric acid was first placed in the test tube and saturated with boron fluoride, after which the anisole was added. The mixture of anisole and catalyst was cooled with an ice-salt mixture to −15°, the liquid pseudobutylene was added, the test tube was sealed, and then heated on the boiling water bath [in the experiments with $BF_3 \cdot O(C_2H_5)_2$] or allowed to stand at room temperature with periodic shaking (in the experiments with $BF_3 \cdot H_3PO_4$). The reaction products were isolated in exactly the same manner as in the experiments with gaseous pseudobutylene.

The most characteristic experiments on the alkylation of anisole with gaseous pseudobutylene in the presence of $BF_3 \cdot H_3PO_4$ (Exps. 1-6) and with BF_3 (Exps. 9 and 10), and also with liquid pseudobutylene in the presence of $BF_3 \cdot H_3PO_4$ (Exps. 7 and 8) and with $BF_3 \cdot O(C_2H_5)_2$ (Exps. 11 and 12), are given in the Table. In Exp. 9 the reaction mixture, after the passage of 13.2 g of pseudobutylene, was allowed to stand overnight at room temperature, after which it was gradually heated to 140°. The boron fluoride evolved here was passed into a receiver containing anhydrous ethyl ether. In this way there was obtained 8.92 g of $BF_3 \cdot O(C_2H_5)_2$, which calculated as free boron fluoride is 4.26 g (67.6%).

Identification of the Products. To identify the alkylation products the wide-boiling fractions collected in the primary distillation from each experiment (being a mixture of sec-butylanisoles), and having close boiling points, specific gravities and refractive indices, were combined and distilled through a fractionation column with an efficiency of 20-25 theoretical plates. The main reaction products were characterized by their physicochemical constants and by their oxidation with nitric acid to methoxyaromatic acids. Their structure was established on the basis of the obtained data. The oxidation was performed as follows: 0.2-0.25 g of the alkylation product was placed in a tube with 15-20 ml of 5% nitric acid. The tube was sealed and heated for 12-16 hours at 130-150°. After cooling the tube was opened, the obtained crystals filtered, and then recrystallized from hot water or ethyl alcohol. In this way the following sec-butylanisoles and methoxyaromatic acids were identified.

Alkylation of Anisole with Pseudobutylene in the Presence of $BF_3 \cdot H_3PO_4$, BF_3 and $BF_3 \cdot O(C_2H_5)_2$

Exp. Nos.	Taken for Reaction (g)				% BF_3 on sum of reactants	Moles of pseudo-butylene per mole of anisole	Reaction conditions		Anisole recovered		Yield of alkylate	
	Anisole	pseudo-butylene	Catalyst				Temper-ature	Time of pseudo-butylene passage (Hrs.)	(g)	(%)	(g)	(%*)
			BF_3	H_3PO_4								
1	27.2	12.8	6.6	10.2	16.5	0.9	Room	3	11.65	42.83	14.85	39.63
2	27.0	17.5	5.5	9.5	12.4	1.2	45-50	4	9.00	33.33	23.20	56.57
3	27.0	16.5	6.4	9.5	14.7	1.2	80-90	1.5	8.33	30.85	26.90	65.59
4	27.1	28.0	3.3	4.8	6.0	2.0	Room	6	20.50	75.65	10.33	25.12
5	27.0	28.3	6.5	9.4	11.7	2.0	Room	4	14.60	54.07	22.93	55.91
6	21.6	28.0	6.5	9.4	13.1	2.5	Room	4	9.35	43.29	24.18	73.70
7	21.6	11.2	6.2	9.4	18.9	1.0	Room	8•	9.53	44.12	12.23	37.29
8	27.3	28.0	6.4	9.4	11.6	2.0	−5−0°	16••	25.10	91.94	3.75	9.04
9	27.0	13.2	6.3	–	15.7	0.9	Room	2	14.95	55.37	15.25	39.47
10	27.2	17.0	10.8	–	24.4	1.2	Room	1.5	6.45	23.71	34.05	82.42
			$BF_3 \cdot O(C_2H_5)_2$									
11	5.5	4.5	0.4		4.0	1.6	100°	16•••	5.26	95.64	0.32	3.83
12	5.5	4.5	0.9		9.0	1.6	100°	4•••	4.27	77.64	2.00	23.96

• In Experiments 1 and 9 the alkylate yield was based on the pseudobutylene, in all of the other experiments – on the anisole.

•• Shaking time for the reaction mixture.

••• Heating time.

o-sec-Butylanisole – colorless oily liquid with a pleasant odor. Its relative amount in the alkylate was 45.5%:

B. p. 76.5-78° (5 mm), d_4^{20} 0.9435, n_D^{20} 1.5029, MR_D 51.06; Calc. 51.20.

0.2066 g sub.: 24.29 g benzene: Δt 0.267°. Found: M 161.5. $C_{11}H_{16}O$. Calculated: M 164.1.

Oxidation with 5% HNO_3 by heating in a sealed tube for 14 hours at 140-150° gave an acid that was obtained as white needle stars or plates, from which o-methoxybenzoic acid with m. p. 101° was isolated by repeated recrystallization from hot water. From the literature, m. p. 98.5-99°.

p-sec-Butylanisole – colorless liquid with a pleasant odor. Its relative amount in the alkylate was 27.4%:

B. p. 81-83° (5 mm), d_4^{20} 0.9374, n_D^{20} 1.5000, MR_D 51.50; Calc. 51.20.

0.2224 g sub.: 23.11 g benzene: Δt 0.302°. 0.4147 g sub.: 23.11 g benzene: Δt 0.575°. Found: M 161.6, 158.2. $C_{11}H_{16}O$. Calculated: M 164.1.

Oxidation with 5% HNO_3 gave p-methoxybenzoic acid as white needles with m. p. 185-187° (from alcohol). From the literature, m. p. 184.2°.

2,4-Di-sec-butylanisole – colorless liquid with a pleasant odor. Its relative amount in the alkylate was 25.1%:

B. p. 129-132° (10 mm), d_4^{20} 0.9143, n_D^{20} 1.4940, MR_D 70.15; Calc. 69.75.

0.2023 g sub.: 23.56 g benzene: Δt 0.207°. 0.4124 g sub.: 23.56 g benzene: Δt 0.427°. Found: M 210.3, 207.9. $C_{15}H_{24}O$. Calculated: M 220.2.

Oxidation with 5% HNO_3 gave 4-methoxyisophthalic acid as white plates with m. p. 257-259° (melts with browning and sublimation).

SUMMARY

1. The alkylation of anisole with pseudobutylene was studied in the presence of the catalysts: BF_3, $BF_3 \cdot H_3PO_4$ and $BF_3 \cdot O(C_2H_5)_2$, at temperatures ranging from −5 to 100°, and for various reactant ratios.

2. It was established that the most effective catalyst for the alkylation of anisole with pseudobutylene is BF_3, the use of which permits obtaining alkylation products in yields as high as 83%, and which can be recovered from the reaction mixture.

3. It was shown that orthophosphoric acid is not essential in the given reaction, and that the catalyst $BF_3 \cdot H_3PO_4$ fails to have any advantage over BF_3.

4. On the basis of the alkylation results it is assumed that anisole, under the studied conditions, is alkylated by pseudobutylene predominantly in the ortho-position.

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REACTION OF AMMONIA WITH 9,10-EPOXYELAIDIC ACID

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In the previous communication [1] we gave the results of studying the reaction between ammonia and 9,10-epoxyoleic acid; here, as was shown, 9-amino-10-hydroxystearic acid is formed.

The present investigation is devoted to a study of the reaction between ammonia and 9,10-epoxyelaidic acid. The epoxyelaidic acid (m. p. 55-55.5°) was prepared by the oxidation of elaidic acid with acetyl hydroperoxide (peroxyacetic acid). The reaction of the epoxy compound with ammonia was run at 130°. A white product with m. p. 188-190° was isolated, which is soluble in dilute alkalies, acids, and in boiling isoamyl alcohol, and insoluble in water, ether, acetone, benzene and chloroform.

Its elementary analysis revealed that here we have a substance with the composition $C_{18}H_{37}O_3N$. The substance fails to evolve ammonia when treated with alkali. Oxidation with sodium periodate is accompanied by ammonia evolution. On the basis of the analysis data and the above-studied properties we concluded that we had obtained a hydroxyaminostearic acid with m. p. 188-190°, having the structure:

$$CH_3(CH_2)_7-\underset{\displaystyle OH}{\underset{|}{CH}}-\underset{\displaystyle NH_2}{\underset{|}{CH}}-(CH_2)_7-COOH \qquad (I)$$

or

$$CH_3(CH_2)_7-\underset{\displaystyle NH_2}{\underset{|}{CH}}-\underset{\displaystyle OH}{\underset{|}{CH}}-(CH_2)_7-COOH \qquad (II)$$

Oxidation of this compound with lead tetraacetate gave pelargonaldehyde (nonanal) (semicarbazone, m. p. 98-100°). In addition to pelargonaldehyde a nitrogen-containing product was isolated, on hydrolysis giving azelaic acid with m. p. 105-106°. On the basis of its obtained oxidation products the hydroxyaminostearic acid should be assigned the structure of 9-amino-10-hydroxystearic acid (I).

For a more detailed study of the hydroxyaminostearic acid we synthesized a number of its derivatives. The hydrochloride, crystallizing as needles, had m. p. 144-145°. Apparently, the hydroxyaminostearic acid hydrochloride obtained by us is analogous to the hydrochloride (m. p. 143-144°) that was isolated by Egorov [2] when he treated oleic and elaidic acids with nitric oxides, followed by reduction with zinc in hydrochloric acid. Egorov failed to elucidate the structure of the compound obtained by him. It appeared sufficient proof to have the NO_2 group and the ester group (ONO) present in the compound. Also, the reduction product of the indicated compound was not studied.

In addition to the hydrochloride, we obtained the hydrochloride of the methyl ester as needles with m. p. 65-66°. The salt is readily soluble in alcohol and acetone, and poorly soluble in ether.

In its physical and chemical properties the indicated hydroxyaminostearic acid is quite different from its analog, obtained from epoxyoleic acid, which can readily be seen when the data given in the Table are compared.

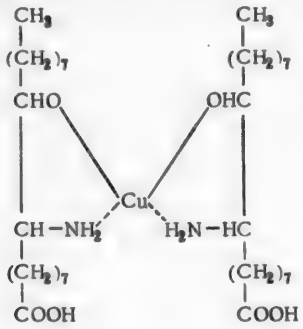
In all probability, the indicated hydroxyaminostearic acids differs from each other in their spatial configuration. Due to the presence of two asymmetric carbon atoms it is possible for two racemic diastereomers to be formed, which, as we can see, differ sharply in their melting points, the same as the two dihydroxyacids. Apparently, the high-melting hydroxyaminostearic acid should be assigned the spatial configuration that corresponds to the OH and NH_2 groups being the greatest distance apart. The low-melting hydroxyaminostearic acid corresponds to that spatial configuration where the OH and NH_2 groups are found the closest to each other.

The reason for making such a conclusion is the fact that the low-melting acid (m. p. 154-155°), when reacted with nitrous acid, is converted into the dihydroxystearic acid with m. p. 100°. In accord with the study made by Esafov*, the formation of the acetone derivative is characteristic for the low-melting dihydroxystearic acid [3]. At

* We obtained analogous results when we repeated Esafov's experiments on the acetonation of the dihydroxystearic acids under identical conditions.

Compound	Melting points of the hydroxyaminostearic acids and their derivatives, obtained from the epoxy acid of	
	Oleic acid	Elaidic acid
Hydroxyaminostearic acid $C_{18}H_{37}O_3N$	154-155°	188-190°
$C_{18}H_{38}O_3NCl$ Hydrochloride	87-89	144-145
Hydrochloride of the methyl ester $C_{19}H_{40}O_3NCl$	61-62	65-66
Copper complex $C_{36}H_{72}O_6N_2Cu$	160-162 (with decomposition)	A complex is not formed

the same time the high-melting dihydroxystearic acid fails to show a tendency to form a similar compound. This postulation on the character of distribution of the OH and NH_2 groups in hydroxyaminostearic acids found its confirmation in the fact that the low-melting hydroxyamino acid gives a complex with copper, i.e. the hydroxy and amino groups are found in a more favorable position for formation of the five-membered ring. The high-melting hydroxyaminostearic acid, having the OH and NH_2 groups in the far position from each other, fails to give the copper complex.



EXPERIMENTAL

Preparation of Epoxyelaidic Acid. The epoxyelaidic acid was obtained by the oxidation of 85.3 g of elaidic acid, dissolved in 400 ml of ether, with an ether solution of acetyl hydroperoxide containing 5.2 g of active oxygen. After recrystallization from petroleum ether and alcohol the obtained epoxide melted at 55-55.5°. The epoxide yield was 95%. Its purity was determined by elementary analysis.

Found %: C 72.54, 72.48; H 11.66, 11.62. Calculated %: C 72.43; H 11.48.

Reaction of Ammonia with Epoxyelaidic Acid. A mixture of 2 g of the epoxide and 15 ml of 35% aqueous ammonia was heated in a sealed tube at 130° for 12 hours. The experiment was repeated 9 times. The ammonia was removed from the contents of the tubes, placed in a porcelain dish, first in the air, and then in vacuo. The obtained precipitate was filtered, washed with water, and then with alcohol and ether. The substance, obtained as a white powder, was insoluble in the ordinary solvents. It was treated at the boil with ethyl alcohol. From 18 g of epoxyelaidic acid there was obtained 18.7 g of hydroxyaminostearic acid. After recrystallization from isoamyl alcohol, m. p. 188-190°.

0.1060 g sub.: 0.2664 g CO_2; 0.1132 g H_2O. 0.0938 g sub.: 0.2354 g CO_2; 0.1008 g H_2O. 0.0669 g sub.: 3.06378 ml N_2. 0.0693 g sub.: 3.14139 ml N_2. 0.1058 g sub.: 0.01872 g KOH. 0.1065 g sub.: 0.01890 g KOH. Found %: C 68.54, 68.44; H 11.95, 12.02; N 4.58, 4.53. M 316.9, 316.1. $C_{18}H_{37}O_3N$. Calculated %: C 68.52; H 11.82; N 4.44. M 315.5.

Oxidation of the Substance with M. P. 188-190° by Sodium Periodate. To 0.04 g of the substance was added 2 ml of 1 N NaOH, 0.3 g of $NaIO_4$, and rapidly 10 ml of saturated K_2CO_3 solution. The liberated ammonia was removed by air-suction with heating to 60-70° for 40 minutes through a system consisting of two cylinders connected in series and containing 1 N hydrochloric acid. The total amount of nitrogen trapped was 1.0458 mg, which represents 59.7% of the theoretical required.

Oxidation with Lead Tetraacetate. To 11 g of hydroxyaminostearic acid in a round-bottomed flask, fitted with thermometer and reflux condenser, was added 90 ml of glacial acetic acid. Then to the acetic acid solution was added 16 g of lead tetraacetate and the mixture heated at 60° for 2 hours. On conclusion of heating the reaction

mixture was diluted with 100 ml of water, and then steam-distilled. From 250 ml of distillate there was extracted 2.7 g of oily substance (54% of the theoretical). The test with fuchsin-sulfurous acid was positive. The Lassen reaction (for nitrogen) gave negative results. With semicarbazide hydrochloride the substance gives a semicarbazone, which after recrystallization from benzene and petroleum ether melted at 98-100°. Its mixed melting point with pelargonaldehyde semicarbazone failed to be depressed.

The residue in the flask (as a thick tar) was treated with steam, thoroughly washed with water, and dried. The substance failed to show the presence of an aldehyde group, but gave the characteristic reaction for nitrogen. The substance was hydrolyzed by heating on the water bath for 20 hours with 50 ml of a 2 N alcoholic potassium hydroxide solution. The copious evolution of ammonia was observed during the hydrolysis. On conclusion of reaction the alcohol was evaporated to dryness; the potassium salt was dissolved in water, neutralized with the calculated amount of dilute hydrochloric acid to slightly acid reaction, and extracted with ether. Removal of the ether gave a brown tarry mass as residue, from which a crystalline substance (2 g) was isolated by treatment with water under heating on the water bath. After recrystallization the substance had m. p. 105-106°. Its mixed melting point with azelaic acid failed to be depressed.

Preparation of the Hydrochloride $C_{18}H_{35}O_3NH_2 \cdot HCl$. To 3 g of the hydroxyaminostearic acid was added 10 ml of dilute hydrochloric acid, containing 0.36 g of HCl. The salt obtained in this manner was filtered and washed with cold water. The precipitate was recrystallized from ethyl acetate. Yield 85%. The salt crystallizes as needles. M. p. 144-145°.

0.2163 g sub.: 0.0878 g AgCl. 0.2158 g sub.: 0.0873 g AgCl. Found %: Cl 10.04, 10.01. $C_{18}H_{38}O_3NCl$. Calculated %: Cl 10.08.

Preparation of the Methyl Ester Hydrochloride $C_{19}H_{37}O_3NH_2 \cdot HCl$. A mixture of 5 g of the hydroxyaminostearic acid and 200 ml of anhydrous methyl alcohol, saturated with hydrogen chloride, in a round-bottomed flask with reflux condenser, was heated on the water bath for 2 hours. On conclusion of heating the hydrogen chloride and methyl alcohol were removed by vacuum-distillation (17 mm) at 16°. To achieve complete HCl removal the flask was treated three times with 50 ml portions of methyl alcohol, and each time the alcohol was removed by vacuum-distillation. The residue, dried over solid KOH in a vacuum-desiccator, became a crystalline mass after standing for two days. The latter, recrystallized from ethyl acetate, was obtained as fine needles with m. p. 65-66°. Yield 60%.

0.2049 g sub.: 0.0799 g AgCl. 0.2807 g sub.: 0.1100 g AgCl. Found %: Cl 9.65, 9.69. $C_{19}H_{40}O_3NCl$. Calculated %: Cl 9.69.

SUMMARY

The reaction of ammonia with epoxyelaidic acid leads to the formation of 9-amino-10-hydroxystearic acid (m. p. 188-190°), being the diastereoisomer (racemate) of the 9-amino-10-hydroxystearic acid (m. p. 154-155°) obtained from epoxyoleic acid. A number of derivatives, characterizing the properties of the hydroxyaminostearic acid, were prepared.

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SYNTHESIS OF THIAZOLIDONE DERIVATIVES WITH BIOLOGICAL INTEREST

I. COMPOUNDS OBTAINED FROM RHODANINE BY SUBSTITUTION IN THE THIO KETONE (THIONO) GROUP

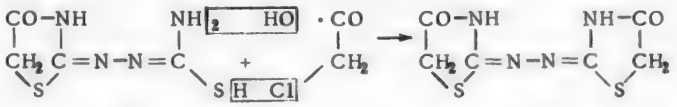
N. M. Turkevich and E. V. Vladzimirskaya

Compounds of 4-thiazolidone have acquired definite biological interest in recent years as substances possessing antithyroid and antitubercular activity. It is also possible that among them will be found compounds possessing anticonvulsant action, which compounds could replace diphenin and nirvanol. The high antithyroid activity established for thiourea [1], pseudohydantoin [2] and rhodanine [3] is associated with the presence of the grouping $>N-\underset{\underset{Y}{\|}}{C}-X-$, where X is sulfur, oxygen or the NH group, and Y is sulfur or the NH group. The indicated grouping is present [4] in the vinylthiooxazolidone molecule, which compound is a natural-occurring antithyroid factor found in the yellow turnip. The solitary 4-thiazolidone derivative found in nature is actithiazic acid [2-(5-carboxypentyl)-4-thiazolidone] (verified), which was isolated [5] as an antibiotic from a strain of stellated fungi (Streptomyces) (verified). Actithiazic acid exhibits high in vitro activity against Mycobacterium tuberculosis.

In this paper we present the synthesis of compounds obtained from rhodanine and containing in their molecules not only the thiazolidone nucleus (and with it also the grouping $>N-\underset{\underset{Y}{\|}}{C}-X-$, characteristic for antithyroid substances), but also the grouping $>C=\underset{|}{N}-\underset{|}{N}-C=$, characteristic [6] for preparations possessing antitubercular activity.

In our previous studies [7-9] it was shown that the $>CS$ group in the rhodanine molecule functions as a thio ketone and is incapable of conversion into the $\rightarrow$ C-SH group, as a result of which rhodanine, analogous to ketones, is capable of forming the phenylhydrazone and oxime. Hydrogen sulfide is evolved when rhodanine is heated with an aqueous-alcohol solution of thiosemicarbazide and the previously unknown rhodanine thiosemicarbazone (I) is formed, which can be regarded as being a combination of pseudothiohydantoin and thiourea, i.e. of two substances possessing antithyroid activity.

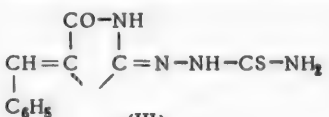
Using the reaction of Wilson and Burns [10], who were the first to show that thiosemicarbazones, analogous to thiourea, when condensed with α-halocarboxylic acids form pseudothiohydantoin derivatives, we attempted to convert rhodanine thiosemicarbazone into the azine. And actually, the condensation of this thiosemicarbazone with chloroacetic acid gave us the rhodanine azine (bis-pseudothiohydantoin) (II):



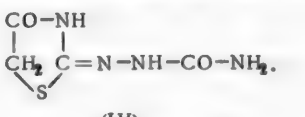
(I) (II)

Heating of the azine, and also of the rhodanine thiosemicarbazone, with concentrated hydrochloric acid gave the thiazolidinedione, which is proof for their proposed structures. The thiazolidine ring in molecules (I) and (II) is more stable than it is in the rhodanine molecule, since solutions of the former in NaOH fail to give the characteristic nitroprusside reaction.

It is possible to obtain 5-benzylidenerhodanine thiosemicarbazone (III) by heating alcohol solutions of thiosemicarbazide and 5-benzylidenerhodanine, but its purification presents considerable difficulties.



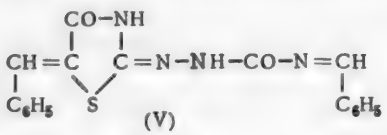
(III)



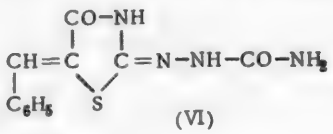
(IV)

Rhodanine with semicarbazide under similar conditions forms rhodanine semicarbazone (IV), up to now obtained [11] in poor yield from chloroacetic acid and monothiohydrazocarboxamide (thioureidourea) $H_2NCSNHNHCONH_2$.

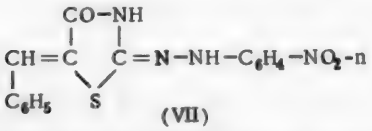
Condensation of the rhodanine semicarbazone with benzaldehyde gave us the dibenzylidene derivative (V). The same compound is also formed in the reaction of benzaldehyde with 5-benzylidenerhodanine semicarbazone (VI), the latter obtained by us in good yield from 5-benzylidenerhodanine and semicarbazide hydrochloride.



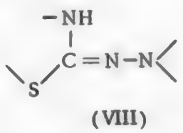
(V)



(VI)



(VII)



(VIII)

The condensation of 5-benzylidenerhodanine with p-nitrophenylhydrazine gave the p-nitrophenylhydrazone (VII), in which molecule, the same as in the chloromycetin molecule, a p-nitrophenyl group is present.

All of the compounds described by us can be regarded as being S-derivatives of the thiosemicarbazide (VIII) (it should be mentioned that the reaction of methyl iodide with thiosemicarbazide yields the S-methylthiosemicarbazide).

The preparations synthesized by us were investigated for their antimicrobial and physiological action. The studies made at the Cathedra of Histology of the Lvov Medical Institute revealed that rhodanine thiosemicarbazone possesses pronounced antithyroid action. It was found that in its degree of goiter production in white rats that rhodanine thiosemicarbazone is 20-25% more active than thiourea, and 10-15% more active than pseudothiohydantoin. The toxidity of the thiosemicarbazone with respect to white rats is slight.

EXPERIMENTAL

Rhodanine Thiosemicarbazone (2,4-Thiazolidinedione 2-Thiosemicarbazone). Ten grams of rhodanine was dissolved in a mixture of 70 ml of alcohol and 70 ml of water, after which it was heated with 10 g of potassium acetate and 7.8 g of thiosemicarbazide under reflux for 12 hours. Hydrogen sulfide was constantly evolved during the whole heating period. The clear solution with reddish tinge was evaporated on the water bath to small volume. The crystalline precipitate was filtered, thoroughly washed with water, and dried. The yield of yellow-orange crystalline powder was 12.3 g (86%). The compound is soluble in alkali solutions, ammonia, and in hot water, slightly soluble in alcohol, and insoluble in ether, acetic acid and benzene. M. p. 196-197° (from water).

20.5 mg sub.: 5.312 ml N_2 (20°, 737 mm). Found %: N 29.28. $C_4H_6ON_4S_2$. Calculated %: N 29.45.

The compound (0.1 g) was heated with 10 ml of concentrated hydrochloric acid on the water bath for 2 hours, after which the liquid was evaporated to small volume. The crystalline precipitate, filtered and then recrystallized from water, had m. p. 124-126° and corresponds to the thiozolidinedione [8].

Rhodanine Azine (2,4-Thiazolidinedione 2-Azine or Bispseudothiohydantoin). A mixture of 3.8 g of rhodanine thiosemicarbazone and 2.5 g of chloroacetic acid was heated with 30 ml of glacial acetic acid under reflux. After refluxing for 30 minutes there was added 50 ml of alcohol, after which the boiling was continued for another 3 hours. The crystalline precipitate was filtered, washed with boiling water, alcohol, ether, and dried. The yield of light-yellow product was 4.5 g (98%). The compound is insoluble in water, alcohol, ether, chloroform and benzene, soluble in alkali solutions and ammonia, and also in concd. HCl. Fails to melt below 300° [11]. Heating with concentrated hydrochloric acid gave the thiazolidinedione, m. p. 125°.

20.2 mg sub.: 4.297 ml N_2 (19°, 740 mm). Found %: N 24.21. $C_6H_6O_2N_4S_2$. Calculated %: N 24.33.

5-Benzylidenerhodanine Thiosemicarbazone (5-Benzyldiene-2,4-thialzolidinedione 2-Thiosemicarbazone). We obtained the 5-benzylidenerhodanine from chloroacetic acid, ammonium thiocyanate and benzaldehyde in one step [12]. A mixture of 5.5 g of 5-benzylidenerhodanine and 2.5 g of thiosemicarbazide in 100 ml of alcohol was heated under reflux for 24 hours. Hydrogen sulfide evolution was observed during the whole reaction period. The small amount of alcohol-insoluble precipitate was filtered, while the filtrate was evaporated to dryness on the water bath. The residue was repeatedly recrystallized from 96% alcohol, 50% alcohol, and glacial acetic acid. A yellow-orange substance was obtained, readily soluble in alcohol and acetic acid, and also in alkali solutions and ammonia, more difficultly soluble in chloroform, ether and benzene, and insoluble in water, and concentrated hydrochloric acid. M. p. 180-186°. Heating with concentrated hydrochloric acid gave the 5-benzylidenethiazolidinedione, m. p. 240° (from alcohol) [8].

22.1 mg sub.: 3.855 ml N_2 (20°, 740 mm). Found %: N 19.79. $C_{11}H_{10}ON_4S_2$. Calculated %: N 20.13.

Rhodanine Semicarbazone (2,4-Thiazolidinedione 2-Semicarbazone). A mixture of 10 g of rhodanine, 10 g of semicarbazide hydrochloride and 15 g of potassium acetate in 75 ml of water was heated under reflux for 15 hours. Here the constant evolution of hydrogen sulfide was observed. The originally homogeneous solution soon deposited a considerable amount of precipitate. After cooling the reaction mixture the precipitate was filtered and recrystallized from water. The yield of the semicarbazone as a white crystalline substance was 12.2 g (93%), soluble in alkali solutions and ammonia, and also in hot water and acetic acid, slightly soluble in alcohol, and insoluble in ether, chloroform and benzene. M. p. 222° with decomposition.

20.5 mg sub.: 5.834 ml N_2 (20°, 737 mm). Found %: N 32.15. $C_4H_6O_2N_4S$. Calculated %: N 32.19.

5-Benzylidenerhodanine Semicarbazone (5-Benzylidene-2,4-thiazolidinedione 2-Semicarbazone). A mixture of 4.4 g of 5-benzylidenerhodanine, 3 g of semicarbazide hydrochloride and 5 g of potassium acetate in 150 ml of alcohol was heated under reflux for 32 hours. Hydrogen sulfide was evolved during the whole reaction time. The boiling mixture was filtered, the precipitate washed with boiling alcohol, and then with water. The yield of yellow substance was 4.7 g (90%), insoluble in water, alcohol, ether, chloroform and benzene, soluble in alkali solutions and ammonia, and more difficultly soluble in acetic acid. M. p. 248° (from acetic acid).

21.0 mg sub.: 3.88 ml N_2 (19°, 739 mm). Found %: N 21.00. $C_{11}H_{10}O_2N_4S$. Calculated %: N 21.36.

5-Benzylidenerhodanine N^4-Benzylidenesemicarbazone (5-Benzylidene-2,4-thiazolidinedione 2-N^4-Benzylidenesemicarbazone). 1) A mixture of 0.52 g of 5-benzylidenerhodanine semicarbazone and 10 ml of benzaldehyde in 200 ml of anhydrous acetic acid was boiled under reflux for 4 hours. The reaction was accompanied by gradual dissolution of the originally insoluble starting substance. After cooling the reaction mixture the crystallized substance was filtered and then recrystallized from alcohol. The yield of substance, colorless with a yellowish tinge, was 0.55 g (80%), insoluble in water and concentrated hydrochloric acid, soluble on heating in alcohol, acetic acid, ether, chloroform, benzene, and alkali solutions. Fails to either melt or change when heated to 265°.

2) A mixture of 0.35 g of rhodanine semicarbazone and 10 ml of benzaldehyde in 200 ml of anhydrous acetic acid was heated at the boil, after which the procedure was the same as indicated above. The yield of substance, identical in its properties with the preceding, was 0.52 g (75%).

18.7 mg sub.: 2.675 ml N_2 (20°, 740 mm). Found %: N 16.23. $C_{18}H_{14}O_2N_4S$. Calculated %: N 15.99.

5-Benzylidenerhodanine p-Nitrophenylhydrazone (5-Benzylidene-2,4-thiazolidinedione 2-p-Nitrophenylhydrazone). A mixture of 1.4 g of the benzylidenerhodanine, 0.97 g of p-nitrophenylhydrazine and 3 g of potassium acetate in 50 ml of alcohol was heated under reflux for 10 hours. The evolution of hydrogen sulfide was observed during the whole reaction period. After cooling the reaction mixture the precipitate was filtered, washed with alcohol, and then water. The yield of dark-brown substance was 1.6 g (74%), insoluble in alcohol, ether, benzene, water and concentrated hydrochloric acid, and difficultly soluble in acetone, nitrobenzene, benzaldehyde and acetophenone. M. p. 233° (from nitrobenzene). The compound is soluble in alkalies and in soda solution with the formation of a red solution. When heated with sodium bicarbonate solution the compound also dissolves with the characteristic red coloration.

20.4 g mg sub.: 2.97 ml N_2 (22°, 740 mm). Found %: N 16.40. $C_{16}H_{12}O_3N_4S$. Calculated %: N 16.46.

SUMMARY

1. Thiosemicarbazide S-derivatives, having the thiazolidone nucleus in their molecule, can be obtained from rhodanine, which behaves like a typical ketone and gives condensation products with phenylhydrazine and its derivatives, hydroxylamine, semicarbazide and thiosemicarbazide.

2. The synthesis of the thiosemicarbazone, semicarbazone and azine of rhodanine was described, and also of the thiosemicarbazone, semicarbazone, benzylidenesemicarbazone and p-nitrophenylhydrazone of 5-benzylidenerhodanine.

3. All of the described substances show acidic properties and are soluble in alkali solutions.

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TABLE 1

β-Aryloxyethanols and Their Properties

Expt. Nos.	Name and formula	Taken for reaction: Phenol (g/mole)	Taken for reaction: $ClCH_2CH_2OH$ (g/mole)	Taken for reaction: NaOH (g/mole)	Taken for reaction: Water (in ml)	Yield (in g)	Yield (in %)	Solvent for Recrystallization	Melting point	Boiling point	d_4^{20}	n_D^{20}	Literature data	Analysis: Weight (in g)	Analysis: 0.1 N $AgNO_3$ required for titration (in ml)	Analysis: Halogen found (in %)	Analysis: Halogen calculated (in %)
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
1	4-Bromophenoxyethanol $BrC_6H_4OCH_2CH_2OH$	21 / 0.121	10 / 0.125	4.85 / 0.121	20	13.9	52.9	Gasoline (b.p. 100-125°)	55°	147-149° (2 mm)	–	–	*	0.2201 0.2356	10.17 10.87	36.93 36.87	36.82
2	2,4-Dichlorophenoxyethanol $Cl_2C_6H_3OCH_2CH_2OH$	163 / 1	88 / 1	44 / 1	300	110	53.2	Benzene	58	185-190 (100 mm)			**	0.1895 0.1761	18.52 17.12	34.65 34.47	34.25
3	2,4,5-Trichlorophenoxyethanol $Cl_3C_6H_2OCH_2CH_2OH$	197.5 / 1	80.5 / 1	40 / 1	500	230.6	80	Gasoline	65					0.1162 0.0918	14.45 11.46	44.08 44.26	44.04
4	2-Methoxyphenoxyethanol $CH_3OC_6H_4OCH_2CH_2OH$	37.2 / 0.3	26.6 / 0.33	12 / 0.3	40	31.7	62.3			163-164 (15 mm)	1.1561	1.5439	***				
5	3-Methoxyphenoxyethanol $CH_3OC_6H_4OCH_2CH_2OH$	37.2 / 0.3	26.6 / 0.33	12 / 0.3	40	39.7	79			143 (5 mm)	1.1531	1.5416	****				
6	2-Ethoxyphenoxyethanol $C_2H_5OC_6H_4OCH_2CH_2OH$	31.4 / 0.227	28.2 / 0.35	9.1 / 0.227	40	23.9	65	Gasoline	38-39	128-130 (2 mm)							
7	3-Propoxyphenoxyethanol $C_3H_7OC_6H_4OCH_2CH_2OH$	12.2 / 0.0803	6.8 / 0.085	3.2 / 0.0803	20	13	83			157 (3 mm)	1.0867	1.5240					
8	4-Propoxyphenoxyethanol $C_3H_7OC_6H_4OCH_2CH_2OH$	19.7 / 0.13	11.3 / 0.14	5.2 / 0.13	40	18.2	70.5	Gasoline and CCl_4	75								
9	3-Butoxyphenoxyethanol $C_4H_9OC_6H_4OCH_2CH_2OH$	13.4 / 0.08	6.8 / 0.085	3.2 / 0.08	20	15.6	84.3			170-172 (5 mm)	1.0591	1.5197					

* M. p. 49-50° [15], 55° [24].

** M. p. 57-58° [27].

*** B. p. 166-167° (22 mm) [13].

**** B. p. 153° (14 mm) [16], 160° (2 mm) [22].

TABLE 1 (continued)

1	2	3	4	5	6	7	8	9	10	11	12	133	14	15	16	17	18
10	4-Propoxy-2-chlorophenoxyethanol $C_3H_7O(Cl)C_6H_3OCH_2CH_2OH$	25.7 0.155	12.9 0.16	6.2 0.155	40	18.4	51.7			169-171 (2 mm)	1.1920	1.5367		0.2642 0.1425	11.54 6.41	15.48 15.60	14.57
11	4-Butoxy-2-chlorophenoxyethanol $C_4H_9O(Cl)C_6H_3OCH_2CH_2OH$	30.5 0.153	12.2 0.153	6.43 0.153	40	24	64.5			171-172 (3 mm)	1.1631	1.5309		0.1711 0.1920	7.02 7.78	14.55 14.38	14.49
12	4-Isopentyloxy-2-chlorophenoxyethanol $C_5H_{11}O(Cl)C_6H_3OCH_2CH_2OH$	16 0.075	6.5 0.08	3 0.075	20	12.5	64.8			191-194 (6 mm)	1.1319	1.5241		0.1632 0.1314	6.50 5.05	13.72 13.63	13.70
13	4-Butoxy-2-bromophenoxyethanol $C_4H_9O(Br)C_6H_3OCH_2CH_2OH$	27 0.11	9.7 0.12	4.4 0.11	40	22	69.2			200-202 (9 mm)	1.3242	1.5433		0.1949 0.2084	6.69 7.18	27.42 27.52	27.64
14	2-Methoxy-4,5-dichlorophenoxyethanol $CH_3O(Cl_2)C_6H_2OCH_2CH_2OH$	11.8 0.06	5.6 0.07	2.44 0.06	20	9.6	66.7	Mixture of gasoline, dichloroethane and CCl_4	94					0.1053 0.1171	8.86 9.95	29.82 30.12	29.91
15	2-Ethoxy-4,5-dichlorophenoxyethanol $C_2H_5O(Cl_2)C_6H_2OCH_2CH_2OH$	13.5 0.0652	5.6 0.07	2.6 0.0652	20	8.2	44.8	Gasoline and CCl_4	77					0.1685 0.1908	13.39 15.35	28.18 28.53	28.24
16	2-Propoxy-4,5-dichlorophenoxyethanol $C_3H_7O(Cl_2)C_6H_2OCH_2CH_2OH$	33 0.15	13 0.16	6 0.15	20	32	73	Dichloroethane and CCl_4	55	177-179 (2 mm)				0.1307 0.1852	9.95 13.71	26.99 26.25	26.75
17	2-Butoxy-4,5-dichlorophenoxyethanol $C_4H_9O(Cl_2)C_6H_2OCH_2CH_2OH$	24.9 0.106	8.8 0.11	4.12 0.106	40	20.5	71.2			180-182 (5 mm)	1.2529	1.5460		0.1668 0.1738	12.09 12.41	25.71 25.31	25.40
18	2-Isopentyloxy-4,5-dichlorophenoxyethanol $C_5H_{11}O(Cl_2)C_6H_2OCH_2CH_2OH$	24.9 0.1	8.8 0.11	4 0.1	40	18.4	62.8			149-152 (2 mm)	1.1918	1.5350		0.2259 0.1801	15.48 12.25	24.30 24.12	24.19
19	2-Methoxy-4,5-dibromophenoxyethanol $CH_3O(Br_2)C_6H_2OCH_2CH_2OH$	28.2 0.1	8.8 0.11	4 0.1	40	23.4	71.8	Mixture of gasoline, dichloroethane and CCl_4	112					0.3264 0.2133	20.18 13.05	49.40 48.91	49.03

TABLE 1 (continued)

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
20	2-Ethoxy-4,5-dibromophenoxyethanol $C_2H_5OC_6Br_2H_2OCH_2CH_2OH$	29.6 0.1	8.8 0.11	4 0.1	40	19.4	57	Gasoline and CCl_4	88					0.2573 0.2161	15.07 12.68	46.80 46.91	47.00
21	2-Propoxy-4,5-dibromophenoxyethanol $C_3H_7OC_6Br_2H_2OCH_2CH_2OH$	26 0.084	6.9 0.85	3.4 0.085	40	23.4	79.7	Gasoline and CCl_4	64-65					0.2718 0.1725	15.34 9.84	45.09 45.56	45.14
22	2-Butoxy-4,5-dibromophenoxyethanol $C_4H_9OC_6Br_2H_2OCH_2CH_2OH$	30.5 0.0941	7.65 0.095	3.76 0.0941	40	18.53	52	Gasoline and CCl_4	53-54	202-204* (6 mm)				0.1278 0.1311	6.93 7.10	43.35 43.28	43.42
23	2-Isophentyloxy-4,5-dibromophenoxyethanol $C_4H_9OC_6Br_2H_2OCH_2CH_2OH$	29.6 0.0873	8 0.1	3.5 0.0873	40	15.3	45.6			180-182 (3 mm)	1.1508	1.5275		0.1213 0.1524	6.46 8.12	42.43 42.57	42.61
24	β-Naphthylmercaptoethanol $C_{10}H_7SCH_2CH_2OH$	40 0.25	18 0.255	10 0.25	500	26.8	52.5	Gasoline	55-56	220-230 (3 mm)				0.1590 0.1125	0.1772* 0.1266*	15.31** 15.45**	15.69**

* Found $BaSO_4$ (in g).

** Amount of S indicated (in %).

EXPERIMENTAL

Preparation of Aryloxyethanols. The aryloxyethanols were prepared under the following conditions. The phenol under heating was dissolved in aqueous sodium hydroxide solution. After the phenol had dissolved, to the heated solution was gradually added ethylene chlorohydrin, and the reaction mixture was boiled under reflux for 2 hours. To the reaction mixture after cooling was added 30-50 ml of 5% sodium hydroxide solution, and the aryloxyethanol was extracted with dichloroethane. The dichloroethane extract was washed with water and dried over anhydrous magnesium sulfate. After distilling off the solvent the residue was either vacuum-distilled or recrystallized from a suitable solvent. The 1-Naphthalenecarbamic acid esters were prepared as follows: equimolar amounts of the alcohol and 1-naphthyl isocyanate were heated for 5-10 minutes on the boiling water bath. The substance obtained after cooling was recrystallized from a suitable solvent and analyzed for its nitrogen content.

Preparation of Aryloxyacetones. To a solution of 0.2 mole of the phenol in 20-40 ml of acetone was added 0.1-0.2 mole of bromoacetone, and then with good stirring was gradually added a solution of 0.1 mole of sodium hydroxide in 20-40 ml of water. After all of the sodium hydroxide had been added the reaction mixture was boiled in a flask under reflux for 10-20 hours. A mechanical stirrer was used to vigorously stir the reaction mixture during the whole reaction time. On conclusion of reaction the mixture was cooled, to it was added 200 ml of 5% aqueous sodium hydroxide solution, and the reaction product was extracted with benzene. The benzene solution was dried over anhydrous magnesium sulfate, and the benzene removed by distillation. The residue was either vacuum-distilled or recrystallized from a suitable solvent. The semicarbazones of the obtained ketones were synthesized in the usual manner.

TABLE 2

Properties of Aryloxyethanol Esters of 1-Naphthalenecarbamic Acid

Expt. Nos.	Name and formula of the 1-Naphthalenecarbamic Acid Ester	Melting Point	Solvent for Recrystallization	Analysis			
				Weight (in g)	0.1 N H_2SO_4 required for titration (in ml)	Found N (in %)	Calculated N (in %)
1	α-Naphthyloxyethyl $C_{23}H_{19}O_3N$	131-132°	Dichloroethane and benzene	0.1358 0.1684	4.01 4.89	4.14 4.06	3.92
2	β-Naphthyloxyethyl $C_{23}H_{19}O_3N$	152	Dichloroethane and benzene	0.1475 0.1248	4.32 3.63	4.10 4.08	3.92
3	2-Methoxyphenoxyethyl $C_{20}H_{19}O_4N$	137-138	Benzene	0.1791 0.2162	5.28 6.29	4.13 4.07	4.15
4	3-Methoxyphenoxyethyl $C_{20}H_{19}O_4N$	107-108	Mixture of benzene with dichloroethane and benzene	0.1460 0.1614	4.43 4.96	4.25 4.30	4.15
5	2-Ethoxyphenoxyethyl $C_{21}H_{21}O_4N$	131-132	Benzene	0.1721 0.1799	4.94 4.95	4.02 3.86	3.99
6	3-Propoxyphenoxyethyl $C_{22}H_{23}O_4N$	120-121	Benzene	0.1424 0.1365	4.17 3.98	4.10 4.08	3.83
7	4-Propoxyphenoxyethyl $C_{22}H_{23}O_4N$	104	Gasoline	0.1404 0.1419	3.93 3.77	3.92 3.72	3.83
8	3-Butoxyphenoxyethyl $C_{23}H_{25}O_4N$	116-117	Mixture of gasoline with benzene	0.1644 0.1757	4.32 4.72	3.68 3.77	3.69

TABLE 3

Aryloxyacetones and their Properties

Expt. Nos.	Name and Formula	Taken for Reaction (g/mole)			Solvent	Yield	
		Phenol	$BrCH_2COCH_3$	NaOH		(in g)	(in %)
1	2-Chlorophenoxyacetone $ClC_6H_4OCH_2COCH_3$	44.5 0.344	24.7 0.18	7.2 0.18	Acetone and water	15	45
2	4-Chlorophenoxyacetone $ClC_6H_4OCH_2COCH_3$	25.7 0.2	13.7 0.1	4 0.1	The same	11.2	60.5
3	2,4-Dichlorophenoxyacetone $Cl_2C_6H_3OCH_2COCH_3$	32.6 0.2	13.7 0.1	4 0.1	" "	11.8	54
4	2,4,5-Trichlorophenoxyacetone $Cl_3C_6H_2OCH_2COCH_3$	19.75 0.1	13.7 0.1	4 0.1	" "	14.5	57.3
5	Pentachlorophenoxyacetone $Cl_5C_6OCH_2COCH_3$	26.6 0.1	13.7 0.1	4 0.1	" "	24.5	80
6	2-Bromophenoxyacetone $BrC_6H_4OCH_2COCH_3$	26 0.11	13.7 0.1	4 0.1	" "	11.5	50.2
7	4-Propoxy-2-chlorophenoxyacetone $C_3H_7O(Cl)C_6H_3OCH_2COCH_3$	27.8 0.15	20.6 0.15	6 0.15	" "	17.4	51
8	4-Butoxy-2-chlorophenoxyacetone $C_4H_9O(Cl)C_6H_3OCH_2COCH_3$	22.1 0.114	15.6 0.114	4.5 0.114	" "	13.6	49
9	2-Ethoxy-4,5-dichlorophenoxyacetone $C_2H_5O(Cl_2)C_6H_2OCH_2COCH_3$	10.3 0.05	6.85 0.05	2 0.05	" "	9.6	73.6
10	2-Butoxy-4,5-dichlorophenoxyacetone $C_4H_9O(Cl_2)C_6H_2OCH_2COCH_3$	11.75 0.05	6.85 0.05	2 0.05	" "	7.7	52.9
11	2-Methoxy-4,5-dibromophenoxyacetone $CH_3O(Br_2)C_6H_2OCH_2COCH_3$	28.2 0.1	13.7 0.1	4 0.1	" "	23.1	68.3
12	2-Ethoxy-4,5-dibromophenoxyacetone $C_2H_5O(Br_2)C_6H_2OCG_2COCH_3$	29.6 0.1	13.7 0.1	4 0.1	" "	19.7	55.6
13	2-Propoxy-4,5-dibromophenoxyacetone $C_3H_7O(Br_2)C_6H_2OCH_2COCH_3$	22.6 0.1	13.7 0.1	4 0.1	" "	25.5	94.5
14	2-Butoxy-4,5-dibromophenoxyacetone $C_4H_9O(Br_2)C_6H_2OCH_2COCH_3$	16.2 0.05	6.85 0.05	2 0.05	" "	15.5	81.7
15	2-Isopentyloxy-4,5-dibromophenoxyacetone $C_5H_{11}O(Br_2)C_6H_2OCH_2COCH_3$	16.9 0.05	6.85 0.05	2 0.05	" "	14.5	73.6
16	β-Naphthylmercaptoacetone $C_{10}H_7SCH_2COCH_3$	16 0.1	13.7 0.1	4 0.1	" "	17.1	79.6

• Found $BaSO_4$ (in g).

•• Amount of S indicated (in %).

Solvent for Recrystallization	Melting point	Boiling point	Literature data	Analysis			
				Weight (in g)	0.1 N $AgNO_3$ required for titration (in ml)	Found Halogen (in %)	Calculated Halogen (in %)
		110-115° (4 mm)		0.1537	8.40	19.05	19.21
				0.1125	6.08	19.17	
Gasoline	57°	168-170 (20 mm)	B.p. 147-148° (17 mm [45]	0.1591	8.53	19.01	19.21
				0.1911	10.3	19.11	
Gasoline	54	138-141 (4 mm)	M.p. 54-55° [46], 55.5-56.5° [47]	0.3069	27.94	32.28	32.37
				0.2664	24.16	32.15	
Mixture of gasoline and benzene	116			0.1479	17.50	41.92	41.96
				0.1136	13.56	42.32	
Methyl alcohol and gasoline	105-105.5		M.p. 106.5 107° [47]	0.2305	35.70	54.91	54.99
				0.2406	36.48	54.85	
		150-155 (10 mm)		0.1524	6.61	34.67	34.88
				0.2523	10.98	34.79	
Gasoline	50	170-172 (3 mm)		0.3404	13.75	14.32	14.61
				0.5262	21.39	14.42	
		174-175 (3 mm)		0.2164	8.61	14.10	13.81
				0.2350	9.29	14.02	
Gasoline and CCl_4	54			0.1566	11.95	27.06	26.95
				0.2030	15.30	26.74	
Gasoline	69	155-158 (3 mm)		0.1339	9.26	24.51	24.35
				0.1911	13.16	24.42	
CCl_4 and a mixture of gasoline with dichloroethane	110			0.2499	14.75	47.18	47.28
				0.3429	20.24	47.16	
Gasoline and CCl_4	72			0.1283	7.26	45.25	45.40
				0.1439	8.16	45.30	
Gasoline and dilute methyl alcohol	71			0.2464	13.39	43.42	43.66
				0.1442	7.84	43.45	
Gasoline and CCl_4	61			0.1284	6.78	42.21	42.05
				0.1674	8.80	42.01	
		198-200 (3 mm)		0.3050	15.54	40.71	40.55
				0.2456	12.50	40.68	
Gasoline and methyl alcohol	135			0.0390	0.0417*	14.70**	14.82**
				0.0438	0.0465*	14.58**	

TABLE 4

Properties of the Semicarbazones of Aryloxyacetones and Arylmercaptoacetones

Expt. Nos.	Semicarbazone	Melting point	Analysis			
			Weight (in g)	0.1 N $AgNO_3$ required for titration (in ml)	Found halogen (in %)	Calculated halogen (in %)
1	2-Chlorophenoxyacetone	171°	0.1290	5.35	14.72	14.67
	$C_{10}H_{12}O_2N_3Cl$		0.2417	10.12	14.85	
2	4-Chlorophenoxyacetone	181-182	0.1107	4.50	14.45	14.67
	$C_{10}H_{12}O_2N_3Cl$		0.1136	4.67	14.58	
3	2,4-Dichlorophenoxyacetone	184-185•	0.0464	3.34	25.52	25.68
	$C_{10}H_{11}O_2N_3Cl_2$		0.1061	7.59	25.37	
4	2,4,5-Trichlorophenoxyacetone	202	0.1381	13.21	33.93	34.25
	$C_{10}H_{10}O_2N_3Cl_3$		0.1570	15.03	33.94	
5	Pentachlorophenoxyacetone	193-194	0.0876	12.01	48.63	48.78
	$C_{10}H_8O_2N_3Cl_5$	(decomp.)	0.0737	10.12	48.69	
6	2-Bromophenoxyacetone	150-151	0.0847	2.96	27.94	27.93
	$C_{10}H_{12}O_2N_3Br$		0.0372	1.29	27.75	
7	4-Bromophenoxyacetone	197••	0.0516	1.80	27.87	27.93
	$C_{10}H_{12}O_2N_3Br$		0.0466	1.63	27.97	
8	2,4,6-Tribromophenoxyacetone	196.5	0.0497	3.35	53.91	54.00
	$C_{10}H_{10}O_2N_3Br_3$		0.0812	5.47	53.85	
9	4-Propoxy-2-chlorophenoxyacetone	147	0.1704	5.04	12.15	11.83
	$C_{13}H_{18}O_3N_3Cl$		0.1503	5.12	12.07	
10	4-Butoxy-2-chlorophenoxyacetone	163	0.2660	8.39	11.19	11.30
	$C_{14}H_{20}O_3N_3Cl$		0.2725	8.58	11.16	
11	2-Ethoxy-4,5-dichlorophenoxyacetone	168-169°	0.1904	17.65	21.70	22.15
	$C_{12}H_{15}O_3N_3Cl$		0.1389	9.05	22.23	
12	2-Butoxy-4,5-dichlorophenoxyacetone	172	0.0507	2.92	20.42	20.36
	$C_{14}H_{19}O_3N_3Cl_2$		0.0426	2.45	20.38	
13	2-Methoxy-4,5-dibromophenoxyacetone	173-174	0.0978	4.99	40.74	40.45
	$C_{11}H_{13}O_3N_3Br_2$		0.1789	9.01	40.25	
14	2-Ethoxy-4,5-dibromophenoxyacetone	176	0.2613	12.70	38.83	39.06
	$C_{12}H_{15}O_3N_3Br_2$		0.1925	9.39	38.97	
15	2-Propoxy-4,5-dibromophenoxyacetone	166.5	0.1156	5.48	37.91	37.77
	$C_{13}H_{17}O_3N_3Br_2$		0.1395	6.61	37.86	
16	2-Butoxy-4,5-dibromophenoxyacetone	172-173	0.1994	9.11	36.51	36.56
	$C_{14}H_{19}O_3N_3Br_2$		0.1934	8.82	36.43	
17	2-Phentyloxy-4,5-dibromophenoxyacetone	171.5	0.1012	4.51	35.63	35.42
	$C_{15}H_{21}O_3N_3Br_2$		0.1718	7.64	35.57	
18	α-Naphthyloxyacetone	196•••	0.1683	19.88••••	16.54•••••	16.33•••••
			0.1724	20.02••••	16.27•••••	
19	2-Benzothiazolylmercaptoacetone [50-53]	182-183	0.1552	22.05••••	19.90•••••	19.99•••••
	$C_{11}H_{12}ON_4S_2$		0.1426	19.97••••	19.95•••••	

• Literature: M. p. 180-181° [46].

•• Literature: M. p. 196-205 [38].

••• Literature: M. p. 103 [33].

•••• Amount of 0.1 N H_2SO_4 required for titration (in ml).

••••• Amount of N (in %).

SUMMARY

1. A number of previously unknown aryloxyethanols and aryloxyacetones were synthesized for the purpose of studying their physiological effect on plants.

2. The testing of the indicated compounds as germination inhibitors for radish and flax seed revealed that some of the aryloxyethanols, containing various substituents in the aromatic radical, are strongly inhibitory.

The aryloxyacetones are completely inactive. The activity of the compounds, all containing the same aromatic radicals, decreases in going from the aryloxyacetic acids to the aryloxyethanols, and then to the aryloxyacetones.

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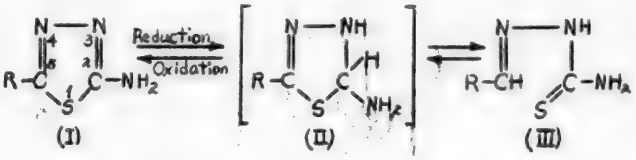
REDUCTION OF THIADIAZOLES WITH RING OPENING

F. F. Medovshchikova and I. Ya. Postovsky

2-Amino-5-alkyl-1,3,4-thiadiazoles (I) are the starting material for the synthesis of bacteriostatic sulfanilamide compounds [1].

It was of interest to obtain the 2,3-dihydro derivatives (II) of these aminothiadiazoles, since such dihydro products appear as though they were cyclic isomers of the thiosemicarbazones (III). As is known, compounds with high antitubercular activity exist among the thiosemicarbazones [2].

The postulation could be made that the dihydro product (II) is also the intermediate substance in the oxidation of the thiosemicarbazones (III) to the 5-alkyl (or aryl)-2-amino-1,3.4-thiadiazoles (I) by the Young method [3].



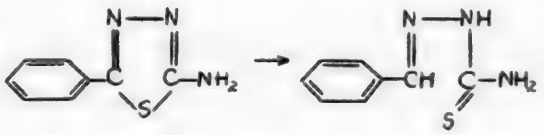
(I) (II) (III)

The possibility of obtaining the dihydro product (II) by the careful oxidation of the thiadiazole (I) was not excluded.

If the dihydro product represents an unstable compound, then it should have given the thiosemicarbazone (III) when cleaved.

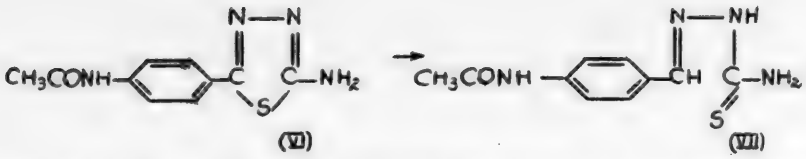
We subjected to reduction the known compounds: 5-phenyl-2-amino-1,3,4-thiadiazole (IV) [4], 5-p-acetaminophenyl-2-amino-1,3,4-thiadiazole (VI) and 5-methyl-2-amino-1,3,4-thiadiazole (IX). It was revealed that these compounds reduce with difficulty: sodium hydrosulfite in alkaline medium, and also zinc dust in alcohol-alkali medium failed to produce any noticeable changes in the taken thiadiazoles. However, when 5% sodium amalgam in alcohol medium (in the cold) was used as the reducing agent there occurred reduction of the heterocycles containing an aromatic radical in the 5 position, while the thiadiazoles with an aliphatic radical in position 5 failed to be reduced under these reaction conditions.

The reduction of 5-phenyl-2-amino-1,3,4-thiadiazole (IV) gave in 50% yield a product with m. p. 154-155°, identical with the thiosemicarbazone of benzaldehyde; the reduction of 5-p-acetylaminophenyl-2-amino-1,3,4-thiadiazole (VI) gave in the same yield a substance with m. p. 221-222°, proving to be the thiosemicarbazone of p-acetylaminobenzaldehyde.*



(IV) (V)

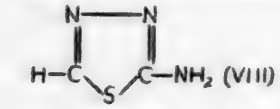
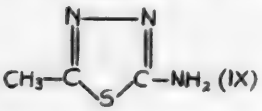
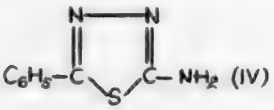
* It is of interest to mention that 5-p-acetylaminophenyl-2-amino-1,3,4-thiadiazole (VI) is without tuberculostatic properties, while the thiosemicarbazone (VII) corresponding to it is a known antitubercular agent.



(VI) (VII)

We assume that the reduction proceeds at the $C^2 - N^3$ bond and that the cyclic dihydro product (II) formed here is cleaved with the formation of the thiosemicarbazone (III), as shown above. It can also be postulated that the reduction fails to proceed at the $C^2 - N^3$, but that under the influence of hydrogen the ring is immediately opened as the result of bond rupture between the C^5 atom and the sulfur atom. However, the latter type of mechanism for explaining the opening of the ring is less probable than the mechanism for opening the ring through the intermediate cyclic dihydro product (II), since the energy of the C – S bond is approximately 24 kcal. greater than for the energy of the π-bond in the group $NH_2-\overset{|}{C}=\overset{|}{N}$.

The difficulty with which the thiadiazoles are reduced, especially those failing to have aromatic radicals in the ring, is also confirmed by the data for the polarographic reduction of certain thiadiazoles, which thiadiazoles are given in the Table.

Thiadiazole	$E_{1/2}$ (V Relative to the Normal Calomel Electrode)
 (VIII)	
 (IX)	
 (IV)	

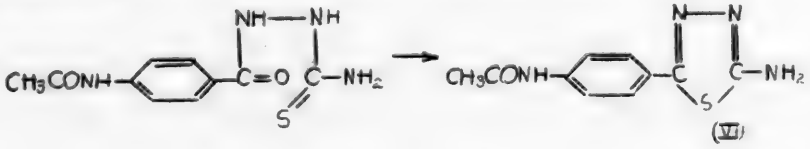
As can be seen from the Table, only the introduction of the aromatic radical into the thiadiazole molecules enables them to be reduced at the mercury dropping electrode.

Attention is drawn to the fact that even 5-phenyl-2-amino-1,3,4-thiadiazole (IV) is reduced only at a high negative half-wave potential, which indicates the difficultly with which the thiadiazole rings are reduced in general.

EXPERIMENTAL

1. Synthesis of Thiadiazoles.- The thiadiazoles used in our work were prepared by methods given in the literature. The thiadiazole (IV) was obtained according to Young by the oxidation of benzaldehyde thiosemicarbazone with ferric chloride under brief boiling [3]. Thiadiazoles (VIII) and (IX) were obtained by the action of acetyl chloride, functioning as a water-removing agent, on the acetyl- and formylthiosemicarbazides, respectively, by the methods described in Freund [5].

The thiadiazole (VI) was obtained by two methods: 1) by the oxidation of p-acetylaminobenzaldehyde thiosemicarbazone with ferric chloride; here satisfactory results are obtained if a solution of ferric chloride is added to a boiling aqueous suspension of the thiosemicarbazone (VII) and the mixture heated for 15 minutes. M. p. 250°, yield 10%; 2) by the ring closure of 1-p-acetylaminobenzoylthiosemicarbazide in the presence of sirupy phosphoric acid as shown in the scheme:



(VI)

Hogarth [6] has described a similar instance of cyclization for other aminothiadiazoles.

Our product had m. p. 250°, and from the analysis data its formula corresponded to that of (VI). The yield was 88%.

Found %: N 23.43. CH_3CO group 1. $C_{10}H_{10}ON_4S$. Calculated %: N 23.85. CH_3CO group 1.

2. Reduction of 5-Phenyl-2-amino-1,3,4-thiadiazole (IV). To a solution of 0.5 g of 5-phenyl-2-amino-1, 3,4-thiadiazole (IV) in 40 ml of alcohol was gradually added with mechanical stirring 26 g (10 times the theoretical) of 5% sodium amalgam in small portions over a period of 1 hour. Then the reaction mixture was stirred another 3.5 hours, after which the alcohol solution was decanted from the unreacted amalgam. After dilution with approximately an equal volume of water and removal of most of the alcohol by distillation, the cooled solution was acidified to slightly acid reaction with 2 N hydrochloric acid.

The resulting colorless crystalline precipitate was filtered, washed with water, and dried. Yield 0.25 g (50%). M. p. 155°. Its mixed melting point with benzaldehyde thiosemicarbazone failed to be depressed.

3. Reduction of 5-p-Acetaminophenyl-2-amino-1,3,4-thiadiazole (VI). To a solution of 0.5 g of the thiadiazole (VI) in 50 ml of alcohol was added in the cold over 40-60 minutes 19.6 g (10-fold excess) of 5% sodium amalgam. All further treatment of the reaction mass was the same as described in the preceding experiment.

From the reaction there was obtained 0.25 g of substance with m. p. 222°. Its mixed melting point with p-acetylaminobenzaldehyde thiosemicarbazone failed to be depressed.

With respect to alkalies, acids, and also solvents, the obtained substance behaves the same as p-acetylaminobenzaldehyde thiosemicarbazone.

4. Polarographic Reduction. A visual polarograph of the U.F.A.N. (Ural Affiliate of the Academy of Sciences) system was used for the polarographic reduction of the thiadiazoles. A weighed amount of the substance being studied was dissolved in a known amount of 0.1 M aqueous-alcohol (60% ethyl alcohol) tetramethylammonium iodide solution. The amount of substance taken was calculated to give a solution with a concentration of 10^{-3} mole/liter.

SUMMARY

1. The reduction of the thiadiazoles (IV) and (VI) to the corresponding thiosemicarbazones (V) and (VII) was described, which method represents a new instance for the opening of heterocycles during reduction.

2. It was established that 2-amino-5-methyl-1,3,4-thiadiazole (IX) is a more stable compound than the 5-aryl substituted derivatives (IV) and (VI); it fails to be reduced by 5% sodium amalgam. The greater stability of 5-methyl-2-amino-1,3,4-thiadiazole to reduction when compared with the 5-aryl derivatives of the aminothiadiazoles is also observed during polarographic reduction.

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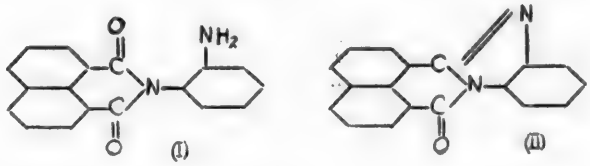
STUDY OF THE PROCESS FOR THE FORMATION OF 1,2-[1',8'-NAPHTHOYLENE] BENZIMIDAZOLE AND ITS AMINOSUBSTITUTED DERIVATIVES

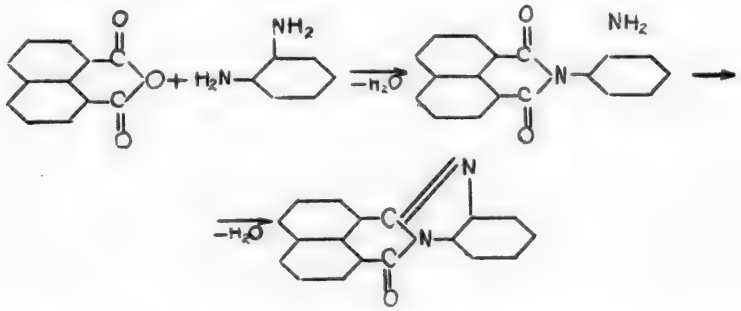
B. M. Krasovitsky and P. M. Matskevich

A method for the preparation of the m- and p-aminophenylimides of naphthalic acid by heating naphthalic anhydride with the nitroanilines in aqueous-alcohol medium in the presence of sodium hydrosulfite has been described by us [1]. Using this method, we wished to obtain under similar conditions the o-aminophenylimide of naphthalic acid; here we obtained two products, of which one (I) proved to be the expected o-aminophenylimide, but in small yield, while the second proved to be identical with the 1,2-[1',8'-naphthoylene] benzimidazole (II), obtained earlier by Bistrzycki [2]:

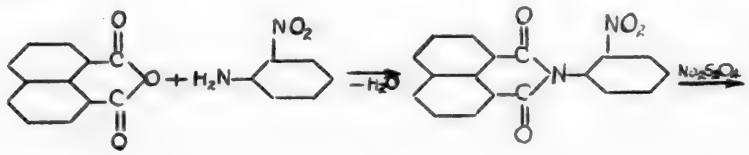


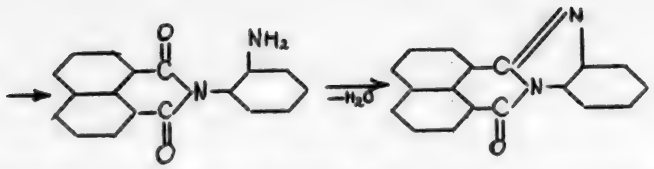
(I) (II)

It could be assumed that the second of these substances is formed in accord with the following scheme: o-nitroaniline is reduced by the hydrosulfite to o-phenylenediamine, which then condenses with naphthalic anhydride to give the o-aminophenylimide of naphthalic acid; the latter, losing one mole of water, is converted into 1,2-[1',8'-naphthoylene] benzimidazole:



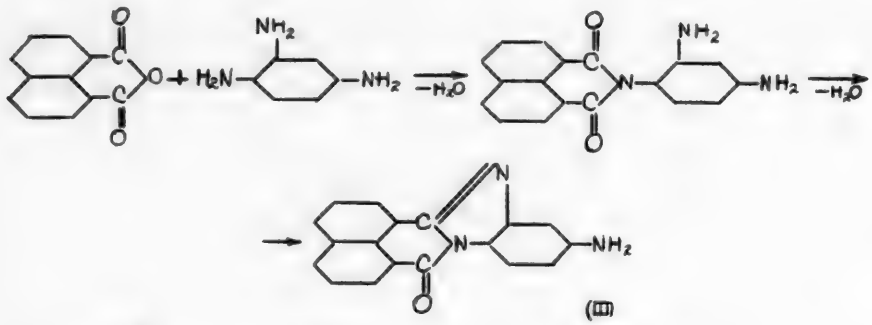
A different scheme for the process is also possible, in accord with which the o-nitrophenylimide is first formed from the naphthalic anhydride and o-nitroaniline, which is then reduced by the sodium hydrosulfite to the aminophenylimide; after one mole of water is cleaved the imidazole ring closes and 1,2-[1',8'-naphthoylene] benzimidazole is formed:



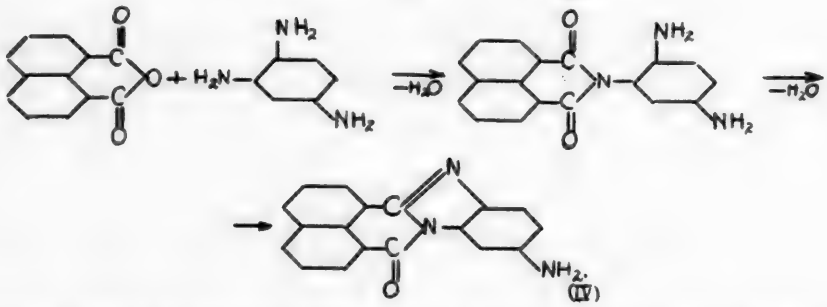


The second of these postulations is the less probable, since naphthalic anhydride in aqueous medium reacts with aniline and its derivatives, containing substituents of the 1st order in the aromatic nucleus, it also reacts with benzidine, but it fails to react with the nitroanilines[3].

If the first scheme is correct and condensation precedes reduction of the nitro compounds, then on heating naphthalic anhydride with 2,4-dinitroaniline in aqueous-alcohol medium in the presence of sodium hydrosulfite the formation of two isomeric products, both containing the imidazole ring (III and IV), should be expected:



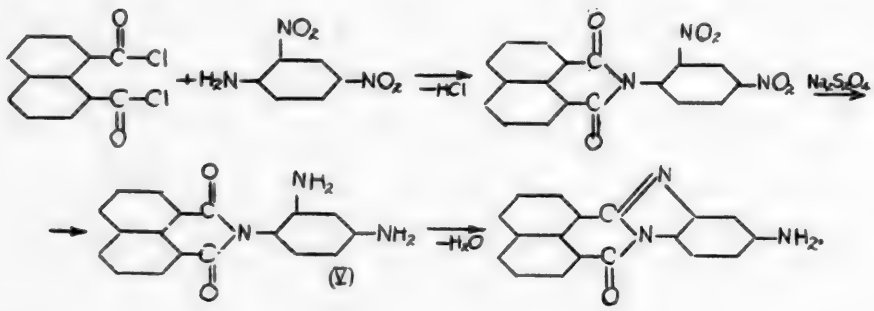
(III)



(IV)

Actually, on running the reaction, we obtained both isomers, of which one, with m. p. 245°, is the more soluble, and the second, with m. p. 275°, is less soluble in dilute hydrochloric acid. The same products were also isolated when we ran the process somewhat differently: we first reduced the 2,4-dinitroaniline with sodium hydrosulfite, and then added the naphthalic anhydride to the formed solution.

In order to establish which of the two obtained products corresponds to formula (III) and which to formula (IV), we effected the synthesis of compound (III) by the following scheme:

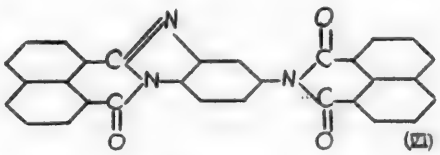


(V)

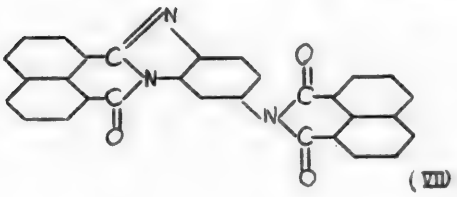
By condensing the acid chloride of naphthalic acid with 2,4-dinitroaniline under the conditions used by one of us for the preparation of the m- and p-nitrophenylimides of naphthalic acid [4], we obtained the 2,4-dinitrophenylimide of naphthalic acid. Reduction of the latter with sodium hydrosulfite in aqueous-alcohol medium gave 4-amino-1,2-[1',8'-naphthoylene]-benzimidazole (III) in extremely small yield, which compound was identical in all its properties with the amine having m. p. 245°, the compound with the greater solubility in hydrochloric acid. As a result, the less soluble product should have the structure corresponding to formula (IV).

Together with the small yield of the 4-amino-1,2-[1',8'-naphthoylene] benzimidazole obtained in the reduction of the 2,4-dinitrophenylimide of naphthalic acid, the main reaction product, apparently, is the 2,4,-diaminophenylimide of naphthalic acid (V), the isolation of which from its admixture with the sodium hydrosulfite decomposition products, due to its extreme solubility and great ease of air-oxidation, we were unable to achieve; we were able to isolate its dibenzoyl derivative, the analysis of which supported the presence of the diamine itself in the reaction products. As a result, the closure of the imidazole ring in the 2,4-diaminophenylimide molecule, obtained in the reduction of the 2,4-dinitrophenylimide, proceeds with greater difficulty than for the preparation of compounds (III) and (IV) from naphthalic anhydride and 1,2,4-triaminobenzene, the latter being formed in the first stage of the process when naphthalic anhydride is heated with 2,4-dinitroaniline in the presence of sodium hydrosulfite.

It should be mentioned that together with the formation of compounds (III) and (IV) a product that is insoluble in dilute hydrochloric acid is formed, in its composition corresponding to the compounds that could have been formed in the condensation of (III) and (IV) with naphthalic anhydride, namely (VI) and (VII):



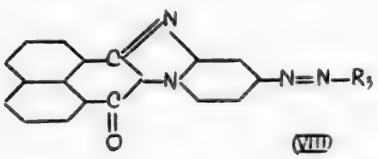
(VI)



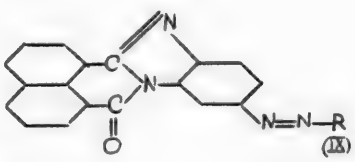
(VII)

We did not study this product in detail. Attempts to synthesize (VI) and (VII) by the condensation of the isolated pure compounds (III) and (IV) with naphthalic anhydride failed to give positive results.

It was interesting to compare the azo dyes from 4-amino-1,2-[1',8'-naphthoylene] benzimidazole (VIII) with the corresponding dyes from 5-amino-1,2-[1',8'-naphthoylene] benzimidazole (IX) and to trace the influence of the position of the azo groups in these dyes on their coloristic properties:



(VIII)



(IX)

R— azo component

Dyes (VIII), as well as dyes (IX), fail to show any affinity for cotton (fiber). As acid dyes they dye wool, where the colors show satisfactory resistance to crocking and boiling, but are poor to perspiration.

EXPERIMENTAL *

N-(o-Aminophenyl)naphthalimide and 1,2,-[1',8'-Naphthoylene]-benzimidazole. A mixture of 4.7 g of naphthalic anhydride, 3.6 g of o-nitroaniline and 50 ml of ethyl alcohol in a flask under reflux was brought to the boil on the water bath, after which 25 ml of water was added to the flask and the heating was continued, with small additions (over 30 minutes) of 7.2 g of sodium hydrosulfite. The heating was continued for 2 hours. The obtained precipitate was filtered from the aqueous-alcohol solution and repeatedly treated under heating to 90° with a 10% soda solution to remove unreacted naphthalic acid. When heated with 3% hydrochloric acid a small part of the precipitate goes into solution, from which the o-aminophenylimide of naphthalic acid separates when ammonia is added.

0.1288 g sub.: 8.9 ml 0.1 N H_2SO_4. 0.1516 g sub.: 10.85 ml 0.1 N H_2SO_4. Found %: N 9.67, 10.02. $C_{18}H_{12}O_2N_2$. Calculated %: N 9.72.

N-(o-Aminophenyl)naphthalimide is a pale yellow powder. M. p. 205°. Yield 0.3 g (4%).

The product, insoluble in 3% hydrochloric acid, was recrystallized from glacial acetic acid. After 3 recrystallizations yellow-green crystals with m. p. 187-189° were obtained. Yield 1.5 g (20%) (the 1,2-[1',8'-naphthoylene] benzimidazole obtained by Bistrzycki had m. p. 189°).

4-Amino-1,2,-[1',8'-naphthoylene] benzimidazole and 5-Amino-1,2-[1',8'-naphthoylene] benzimidazole.

a) A mixture of 6.8 g of 2,4-dinitroaniline and 5 g of naphthalic anhydride was suspended in 70 ml of alcohol with heating on the boiling water bath. Then 35 ml of water was added and 28 g of sodium hydrosulfite was sifted in. Heating was continued for 5 hours. The alcohol was distilled off, the precipitate was filtered, and then it was treated with 10% soda solution under heating to remove unreacted naphthalic acid. The reaction product was a mixture of substances that were soluble and insoluble in dilute hydrochloric acid.

b) The condensation was run with the same quantities of reactants as before, but the naphthalic anhydride was added after the introduction of the sodium hydrosulfite; in this case also, after distilling off the alcohol and treating the precipitate with soda solution, there remains a mixture of substances that are soluble and insoluble in dilute hydrochloric acid.

Separation of the Products Soluble in Dilute Hydrochloric Acid. 1) The reaction product was repeatedly treated in the cold with 6% hydrochloric acid until the extracts failed to give a precipitate when ammonia was added. The combined hydrochloric acid extracts were treated with ammonia and the precipitated amine was purified by repeated solution in hydrochloric acid and subsequent precipitation with ammonia. The amine was a brick-red product with m. p. 245-247° (when the capillary was dropped into the bath heated to this temperature). Yield 1.9 g (26.4%).

0.0932 g sub.: 9.6 ml 0.1 N H_2SO_4. 0.1490 g sub.: 15.4 ml 0.1 N H_2SO_4. Found %: N 14.42, 14.50. $C_{18}H_{11}ON_3$. Calculated %: N 14.73.

0.1034 g sub.: 3.75 ml 0.1 N $NaNO_2$. 0.1025 g sub.: 3.70 ml 0.1 N $NaNO_2$.** Found %: $C_{18}H_9ON_2(NH_2)$ 103.6, 103.0.

2) The product, remaining after treatment with cold 6% hydrochloric acid, was heated with the same concentration of acid. The hot hydrochloric acid extract was poured into ammonia; the resulting amine precipitate of yellow-brown color was purified by repeated solution in hydrochloric acid and subsequent precipitation with ammonia. Yield 1.0 g (13.9%). M. p. 275°.

0.1513 g sub.: 15.7 ml 0.1 N H_2SO_4. 0.1301 g sub.: 13.5 ml 0.1 N H_2SO_4. Found %: N 14.53, 14.52. $C_{18}H_{11}ON_3$. Calculated %: N 14.73.

0.1015 g sub.: 3.45 ml 0.1 N $NaNO_2$. 0.1199 g sub.: 4.25 ml 0.1 N $NaNO_2$. Found %: $C_{18}H_9ON_2(NH_2)$ 96.9, 100.9.

Both here and in the preceding instance the nitrogen analysis and the amino group determinations both support the formation of aminoimidazole derivatives.

3) The precipitate, insoluble in 6% hydrochloric acid, was analyzed for nitrogen:

* Students E. Yu. Rokhlenko and N. I. Titarenko from the Kharkov State University assisted in the experimental portion of this work.

** The course of the diazotization was controlled with the aid of iodide starch paper.

0.1776 g sub.: 11.35 ml 0.1 N H_2SO_4. Found %: N 8.95. $C_{30}H_{15}O_3N_3$. Calculated %: N 9.03.

Thus, the composition of the analyzed substance corresponds to formulas (VI) and (VII). We failed to study this product in greater detail.

N-(2,4-Dinitrophenyl)naphthalimide. The naphthaloyl chloride needed for the work was obtained by the reaction of naphthalic anhydride with phosphorus pentachloride [5]. A mixture of 14 g of naphthaloyl chloride (m. p. 86°) and 11 g of 2,4-dinitroaniline was heated on the water bath for 5 hours in anhydrous benzene. The precipitate was purified by heating with 10% aqueous soda solution, and then with alcohol. Yield 10 g (50%).

The reaction product, a yellow powder with m. p. 210°, is insoluble in water, glacial acetic acid, ethyl alcohol, toluene, xylene and butyl acetate.

0.1553 g sub.: 12.60 ml 0.1 N H_2SO_4. 0.1116 g sub.: 8.95 ml 0.1 N H_2SO_4. Found %: N 11.36, 11.22. $C_{18}H_9O_6N_3$. Calculated %: N 11.57.

Reduction of N-(2,4-Dinitrophenyl)naphthalimide. The N-(2,4-dinitrophenyl)naphthalimide (5 g) was suspended with heating in 50 ml of ethyl alcohol and then 25 ml of water was added. Then, with continued heating on the boiling water bath, 20 g of sodium hydrosulfite was added in small portions over 30 minutes, after which the heating was continued for another 5 hours. After distilling off the alcohol a small amount of the amine deposited, which after two purifications by the method of dissolving in hydrochloric acid and then precipitating with ammonia, melted at 245-246° (when the capillary was dropped into the bath heated to this temperature). The filtrate was evaporated and hydrochloric acid was added to it in the cold. A small amount of precipitate was obtained (apparently, the sulfamino derivative), which dissolved when heated with hydrochloric acid (hydrolysis of the sulfamino derivative) to give the amine as precipitate when ammonia was added, which amine after purification had m. p. 245-246°. Total yield of amine 0.11 g (2.8%).

0.1026 g sub.: 3.65 ml 0.1 N $NaNO_2$. 0.1130 g sub.: 3.9 ml 0.1 N $NaNO_2$. Found %: $C_{18}H_9ON_2(NH_2)$ 101.4, 98.5.

As a result, the obtained substance contains one amino group and is 4-amino-1,2[1',8'-naphthoylene] benzimidazole, identical with product (III). A brownish filtrate was always obtained after isolation of the 4-amino-1,2-[1',8'-naphthoylene] benzimidazole, which filtrate gradually turned dark. By evaporating this filtrate and treating it with benzoyl chloride, by the Schotten-Baumann reaction, we obtained a substance, which after repeated washing with water and recrystallization from aqueous alcohol, had m. p. 207-209°, and which from its nitrogen content corresponded to the dibenzoyl derivative of N-(2,4-diaminophenyl)naphthalimide:

5.920 mg sub.: 0.415 ml N_2 (23°, 737 mm). Found %: N 7.84. $C_{32}H_{21}O_4N_3$. Calculated %: N 8.22.

Dyes from 4-Amino-1,2-[1',8'-naphthoylene] benzimidazole and 5-Amino-1,2-[1',8'-naphthoylene] benzimidazole. A solution of 0.5 g of the amine in 6 ml of 6% hydrochloric acid was diazotized at 0-5° with 0.12 g of sodium nitrite. Sodium acetate was added to the diazo solution to bind the excess hydrochloric acid and then the diazo was coupled with 1-hydroxy-8-aminonaphthalene-3,6-disulfonic acid (0.56 g) and 2-naphthol-3,6-disulfonic acid (0.61 g). The dyes were purified by dissolving in water and then salting them out with sodium

Diazo Component	Azo Component					
	1-Hydroxy-8-aminonaphthalene-3,6-disulfonic Acid			2-Naphthol-3,6-disulfonic Acid		
	Crocking	Perspiration	Boiling	Crocking	Perspiration	Boiling
4-Amino-1,2-[1',8'-naphthoylene] benzimidazole	4/4/3	3/4/1	4/4/4	4/4/4	4/4/3	4/4/4
5-Amino-1,2-[1',8'-naphthoylene] benzimidazole	4/4/3	3/4/1	4/4/4	4/4/3	3/4/2	4/4/4

acetate, which contamination was then removed by heating the dye with alcohol. The shades, obtained in the dyeing of wool with the dyes obtained from 4-amino-1,2-[1',8'-naphthoylene] benzimidazole, differed but slightly in color and resistance to wet treatments from the dyes obtained from 5-amino-1,2-[1',8'-naphthoylene] benzimidazole. The data on the resistance of the colors to crocking, perspiration and boiling are given in the Table.

SUMMARY

1. The heating of naphthalic anhydride with o-nitroaniline in aqueous-alcohol medium in the presence of sodium hydrosulfite gave 1,2-[1',8'-naphthoylene] benzimidazole.

2. The heating of naphthalic anhydride with 2,4-dinitroaniline in aqueous-alcohol medium in the presence of sodium hydrosulfite gave 4-amino-1,2[1',8'-naphthoylene] benzimidazole and 5-amino-1,2-[1',8'-naphthoylene] benzimidazole.

3. The azo dyes from the amino derivatives of 1,2-[1',8'-naphthoylene] benzimidazole dye wool in an acid bath; the colors possess satisfactory resistance to crocking and boiling, but show poor resistance to perspiration.

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CYANINE DYES

IX. SOME TETRAMETHOXYTHIACARBOCYANINES

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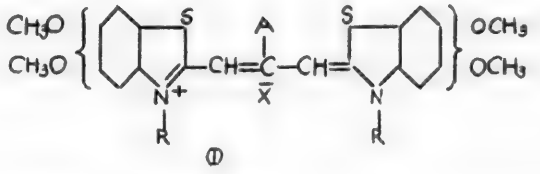
In one of our previous studies it was shown that in the transition from the di- to the tetramethylthiacarbocyanines a noticeable bathochromic shift in the absorption maximum of the dye is observed, in which connection the influence of substituents on the color is additive [1]. It seemed expedient to also study the properties of carbocyanines with two substituents in different positions on the hetero rests, the two substituents possessing a greater polarity and therefore showing a greater influence on the position of the absorption maximum of the dye.

In this connection we synthesized and studied a number of 4,5,4',5'-, 4,6,4',6'-, 4,7,4',7'- and 5,6,5',6'-tetramethoxythiacarbocyanines (I).



(I)

A = H, CH_3 or C_2H_5; R = CH_3 or C_2H_5; X = acidic radical.

Of these dyes a number of the 5,6,5',6'-tetramethoxy derivatives are given in several patents [2] and their use as optical sensitizers for silver halide emulsions is proposed [3]. In these patents it is indicated that the introduction of methoxy groups in the 5,6,5',6'-positions causes a noticeable shift of the absorption maximum in thiacarbocyanines toward the long-wave portion of the spectrum.

TABLE 1

Absorption Maxima of 3,3'-Diethyltetramethoxythiacarbocyanines

Position of the Methoxy Groups	Substituents in the 9 Position		
	H	CH_3	C_2H_5
–	558	543	547
4,5,4',5'	572	550	555
4,6,4',6'	574	562	565
4,7,4',7'	564	548	552
5,6,5',6'	596	575	580

The starting 5,6- and 4,7-dimethoxy-2-methylbenzothiazoles, described earlier by Fries [4, 5], and also the 4,5- and 4,6-dimethoxy derivatives, were obtained by us by the oxidation of the thioacetyl derivatives of the corresponding aminodimethoxybenzenes with potassium ferricyanide (cf. [6]).

The oxidation of 4-thioacetamino-1,3-dimethoxybenzene yielded appreciable amounts of the corresponding disulfide, which we were able to isolate in the pure state.

The dyes were synthesized by heating the reacting alkyl-p-toluenesulfonates of the dimethoxy-2-methylbenzothiazoles with the ortho esters of carboxylic acids in pyridine (cf. [7]) and were isolated as well-crystallized iodides.

The absorption maxima of the obtained 3,3'-diethyltetramethoxythiacarbocyanines (in ethyl alcohol) are given in Table 1.

TABLE 2

Name of dyes	Amount of free base (in g)	Amount of p-toluene-sulfonic acid ester (in g)	Ortho ester*	Amount of ortho ester (in g)	Amount of pyridine (in ml)	Yield (in % of the theoretical)
3,3'-Diethyl-4,5,4',5'-tetramethoxythiacarbocyanine Iodide	0.21	0.21	OE1	0.30	2.0	75
3,3'-Diethyl-9-methyl-4,5,4',5'-tetramethoxythiacarbocyanine Iodide	0.21	0.21	OE2	0.33	2.0	38
3,3',9-Triethyl-4,5,4',5'-tetramethoxythiacarbocyanine Iodide	0.21	0.21	OE3	0.36	2.0	31
3,3'-Dimethyl-9-ethyl-4,5,4',5'-tetramethoxythiacarbocyanine Iodide	0.21	0.20	OE3	0.36	2.0	62
3,3'-Diethyl-4,6,4',6'-tetramethoxythiacarbocyanine Iodide	0.21	0.21	OE1	0.30	1.0	55
3,3'-Diethyl-9-methyl-4,6,4',6'-tetramethoxythiacarbocyanine Iodide	0.21	0.21	OE2	0.32	1.0**	33
3,3',9-Triethyl-4,6,4',6'-tetramethoxythiacarbocyanine Iodide	0.21	0.21	OE3	0.26	1.0**	42
3,3'-Dimethyl-9-ethyl-4,6,4',6'-tetramethoxythiacarbocyanine Chloride	0.21	0.20	OE3	0.26	1.0**	38
3,3'-Diethyl-4,7,4',7'-tetramethoxythiacarbocyanine Iodide	0.42	0.42	OE1	0.60	2.5	75
3,3'-Diethyl-9-methyl-4,7,4',7'-tetramethoxythiacarbocyanine Iodide	0.42	0.42	OE2	0.64	2.5	35
3,3',9-Triethyl-4,7,4',7'-tetramethoxythiacarbocyanine Iodide	0.42	0.42	OE3	0.70	3.0	23.5
3,3'-Dimethyl-9-ethyl-4,7,4',7'-tetramethoxythiacarbocyanine Iodide	0.42	0.40	OE3	0.70	3.0	34
3,3'-Diethyl-5,6,5',6'-tetramethoxythiacarbocyanine Iodide	0.42	0.42	OE1	0.60	2.5	78
3,3'-Diethyl-9-methyl-5,6,5',6'-tetramethoxythiacarbocyanine Iodide	0.42	0.42	OE2	0.64	3.0	46
3,3',9-Triethyl-5,6,5',6'-tetramethoxythiacarbocyanine Iodide	0.42	0.42	OE3	0.70	3.0	34
3,3'-Dimethyl-9-ethyl-5,6,5',6'-tetramethoxythiacarbocyanine Iodide	0.42	0.40	OE3	0.70	3.0	30

* OE1 – ethyl orthoformate, OE2 – ethyl orthoacetate, OE3 – ethyl orthopropionate.

** 0.10 g of acetic anhydride was added.

*** The amount of N is given.

These data, part of which were briefly published by us earlier [9], show that the transition from the di- [8] to the tetramethoxythiacarbocyanines in the case of the 4,6,4',6'-, 4,7,4',7'- and 5,6,5',6'-derivatives results in deepening of the color, while at the same time the absorption maximum for the 4,5,4',5'-tetramethoxy derivatives lies between the absorption maxima for the 4,4'- and 5,5'-dimethoxythiacarbocyanines.

It should be mentioned that the bathochromic effect produced as the result of introducing methoxy groups in the 5,6,5',6'-positions of these dyes is somewhat greater than the sum of the shifts produced by the substituents in the corresponding dimethoxythiacarbocyanines (38 $m\mu$ versus 32 $m\mu$).

External appearance	Melting point	Absorption maximum in mμ (in C_2H_5OH)	Analysis		
			Found	Calculated	
			I (%)	Formula	I (%)
Red needles with greenish case	223-224°	572	20.85	$C_{25}H_{29}O_4N_2S_2I$	20.73
Dark-green prisms	215-217	550	20.39	$C_{26}H_{31}O_4N_2S_2I$	20.27
Dark-green prisms	202-203	555	20.01	$C_{27}H_{33}O_4N_2S_2I$	19.82
Red prisms	206-208	552	20.89	$C_{25}H_{29}O_4N_2S_2I$	20.73
Purple prisms	248-250	574	4.64•••	$C_{25}H_{29}O_4N_2S_2I$	4.57•••
Bluish-purple prisms	224-225	562	4.52•••	$C_{26}H_{31}O_4N_2S_2I$	4.47•••
Brown prisms with greenish cast	222-223	565	4.46•••	$C_{27}H_{33}O_4N_2S_2I$	4.37•••
Lustrous brown prisms with greenish cast	174-176	562	5.49•••	$C_{25}H_{29}O_4N_2S_2Cl$	5.37•••
Bluish-purple needles	224-225	564	20.88	$C_{25}H_{29}O_4N_2S_2I$	20.73
Brownish-red crystals	206-207	548	20.39	$C_{26}H_{31}O_4N_2S_2I$	20.27
Green leaflets with golden luster	210-212	552	19.68	$C_{27}H_{33}O_4N_2S_2I$	19.82
Reddish-purple needles	210-211	550	20.62	$C_{25}H_{29}O_4N_2S_2I$	20.73
Green prisms	249-250	596	20.86	$C_{25}H_{29}O_4N_2S_2I$	20.73
Bluish-purple prisms	241-242	575	20.42	$C_{26}H_{31}O_4N_2S_2I$	20.27
Blue needles with a steel luster	222-223	580	19.93	$C_{27}H_{33}O_4N_2S_2I$	19.82
Brownish-red prisms	236-237	576	20.82	$C_{25}H_{29}O_4N_2S_2I$	20.73

The abnormally heightened color of the 4,5,4',5'-tetramethoxythiacarbocyanines can possibly be associated with stearic difficulties involved in the electron reaction of the methoxy groups with the polymethine chromophore (cf. [10, 11]).

The space models of these dyes, constructed with the interatomic distances and valence angles taken into consideration, show that in them the methoxy groups and the hydrocarbon radical on the nitrogen atom cannot lie in the same plane. In association with this in the 4,5,4',5'-tetramethoxythiacarbocyanines the electron shifts from the methoxy groups are apparently weakened, which should lead to a heightening of the color (cf. [10-13]).

The investigated tetramethoxythiacarbocyanines are average in their properties as optical sensitizers. The least sensitizing ability is possessed by the 4,7,4',7'-derivatives, which, possibly, is associated with the presence of substituents in the 7,7'-positions (cf. [8]). The ability of the investigated tetramethoxythiacarbocyanines for 2nd order sensitization is quite weakly expressed [14].

EXPERIMENTAL

(Jointly with Z. Ya. Bukshpan)

3-Acetaminoveratrole. Obtained by a slight modification of the Vermeulen method [15]. A mixture of 4.6 g of freshly distilled 3-aminoveratrole and 6.4 ml of acetic anhydride was allowed to stand; the next day the reaction mixture was diluted with 40 ml of water, cautiously neutralized with soda, the product filtered, washed with water, and dried. Yield 5.4 g (95%). M. p. 82-83° (according to Vermeulen [15], m. p. 84°). Colorless prisms (from dilute alcohol).

To obtain the starting 3-aminoveratrole, m-nitroanisole was nitrated with nitric acid (d 1.5) to give the 2,3-dinitroanisole [16], which with sodium methylate [17] was converted into 3-nitroveratrole. The latter was then reduced with iron in weakly acid medium [18].

3-Thioacetamino-1,2-dimethoxybenzene. To a solution of 1.95 g of 3-acetaminoveratrole in 20 ml of boiling dry benzene was gradually added 0.56 g of finely ground phosphorus pentasulfide. Then the mixture was boiled under reflux for 25 minutes, the benzene solution was decanted from the tarry deposit and the latter was washed with 20 ml of benzene, which was added to the main solution. The benzene solution was shaken with 80 ml of 5% sodium hydroxide solution [in 4 portions (doses)]. The alkaline solution was neutralized with acetic acid, and the thioacetyl derivative was isolated by the passage of carbon dioxide gas. The pale yellow precipitate was filtered, washed with water, and dried. Yield 0.72 g (34%). M. p. 76-78°. For analysis the product was recrystallized from ethyl alcohol. Almost colorless needles, M. p. 81°.

Found %: N 6.58, 6.71. $C_{10}H_{13}O_2NS$. Calculated %: N 6.63.

4-Thioacetamino-1,3-dimethoxybenzene. Obtained in the same manner as the previous compound from 19.5 g of 4-acetamino-1,3-dimethoxybenzene (m. p. 114-115° [19]) by heating with 11.0 g of phosphorus pentasulfide in 300 ml of dry benzene for 2 hours. The thioacetyl derivative was extracted from the benzene solution by shaking with a 2% sodium hydroxide solution (10 times with 200 ml portions). Yield 51%. M. p. 88-89°. Pale yellow lustrous prisms (from ethyl alcohol, 1:5). M. p. 89-90°.

Found %: N 6.81. $C_{10}H_{13}O_2NS$. Calculated %: N 6.63.

2-Methyl-4,5-dimethoxybenzothiazole. A solution of 4.2 g of 3-thioacetaminoveratrole in 42 ml of 8% potassium hydroxide solution at 0-5° was gradually added with stirring to a solution of 13.2 g of potassium ferricyanide in 65 ml of water. The next day the liquid was extracted with ether, the extract dried over potash, the ether distilled off, and the residue (3.2 g) converted to the picrate in alcohol solution (3.7 g of picric acid in 10 ml of alcohol). The insoluble picrate was filtered and thoroughly washed with ether. Yield 5.4 g (61%). Decomposition of the picrate with aqueous soda solution gave 2.25 g of the free base as yellowish crystals with m. p. 56-58°. For purification the latter were recrystallized twice from gasoline. Colorless prisms with m. p. 61.5-62°. Readily soluble in alcohol and benzene, and quite difficultly soluble in cold ligroine.

Found %: N 6.79. $C_{10}H_{11}O_2NS$. Calculated %: N 6.70.

Picrate – yellow prisms (from ethyl alcohol). M. p. 129-130°.

Found %: N 12.87. $C_{16}H_{14}O_9N_4S$. Calculated %: N 12.78.

2-Methyl-4,6-dimethoxybenzothiazole. A filtered solution of 4.22 g of 4-thioacetamino-1,3-dimethoxybenzene and 2.4 g of sodium hydroxide in 60 ml of 30% ethyl alcohol was added with stirring over 30 minutes at 0-5° to a solution of 13.2 g of potassium ferricyanide in 90 ml of water. The next day the obtained precipitate was extracted with ether, and the ether extracted was repeatedly shaken with 10% hydrochloric acid (4 times with 50 ml portions). The acid water solution was made alkaline to give the free base as a nearly colorless precipitate. Yield 1.30 g (31%). M. p. 53-55°.

Colorless prisms (from gasoline with b. p. 60-70°). M. p. 58-59°. Very easily soluble in alcohol, ether and benzene, and somewhat less soluble in gasoline.

Found %: N 6.71. $C_{10}H_{11}O_2NS$. Calculated %: N 6.69.

Picrate – pale yellow prisms (from alcohol, 1:30). M. p. 173-174°.

The ether solution after extracting the free base was washed with 2% sodium hydroxide solution and water, dried over sodium sulfate, and the ether distilled off to leave a brown residue that completely crystallized on cooling. Weight 1.81 g (43%). M. p. 74-76°. Colorless needles (from ethyl alcohol, 1:4). M. p. 84-85°. Insoluble in aqueous alkalies and acids at room temperature. Readily soluble in alcohol and benzene.

Found %: N 6.55, 6.50. $C_{20}H_{24}O_4N_2S_2$. Calculated %: N 6.66.

Sulfur and hydrogen sulfide were liberated when 0.5 g of the substance was boiled for 30 minutes with 5 ml of 20% hydrochloric acid. A nearly colorless precipitate was obtained when 0.6 g of acetic anhydride was added to the soda-neutralized solution, which after recrystallization from dilute alcohol had m. p. 114-115°, and which failed to show a melting point depression when mixed with 4-acetamino-1,3-dimethoxybenzene.

2-Methyl-4,7-dimethoxybenzothiazole. Synthesized in the same manner as the preceding compound from 2-thioacetamino-1,4-dimethoxybenzene, with purification through the picrate. Yield 75%. Colorless needles (from ethyl alcohol). M. p. 100-101° (Fries [5] gives m. p. 101°).

Picrate – yellow needles (from ethyl alcohol). M. p. 155-156°.

Methiodide. A mixture of 0.42 g of 2-methyl-4,7-dimethoxybenzothiazole and 0.28 g of methyl iodide was heated for 5 hours on the boiling water bath in a flask under reflux; then 0.14 g of methyl iodide was added, and the heating was continued for another 5 hours. The crystalline mass was washed with benzene and boiling acetone. Yield 81%. Slightly grayish prisms (from anhydrous ethyl alcohol), M. p. 209-210°.

Found %: I 36.24. $C_{11}H_{14}O_2NSI$. Calculated %: I 36.15.

The Ethiodide was obtained in the same manner as the preceding compound; the duration of heating was increased to 20 hours. Yield 88%. Grayish needles (from ethyl alcohol . M. p. 221-222°.

Found %: N 3.92, 3.95. $C_{12}H_{16}O_2NSI$. Calculated %: N 3.84.

The Propiodide was obtained by heating 2-methyl-4,7-dimethoxybenzothiazole with a 20% excess of propyl iodide at 110-120° for 15 hours. Yield 63%. Slightly greenish needles (from anhydrous ethyl alcohol). M. p. 186-187°.

Found %: I 33.56, 33.62. $C_{13}H_{18}O_2NSI$. Calculated %: I 33.48.

The Methyl-p-toluenesulfonate – nearly colorless find needles (from acetone). M. p. 149-150°.

Found %: S 16.35. $C_{18}H_{21}O_5NS_2$. Calculated %: S 16.22.

2-Methyl-5,6-dimethoxybenzothiazole. Obtained by the Fries method [4] of oxidizing 4-thioacetaminoveratrole with potassium ferricyanide. Colorless crystals (from ethyl alcohol). M. p. 75-76° (literature m. p. 75°[4]).

Picrate – yellow prisms (from ethyl alcohol, 1:100). M. p. 204-205°.

Tetramethoxythiacarbocyanines. To obtain the 3,3'-diethyltetramethoxythiacarbocyanines the dimethoxy-2-methylbenzothiazoles were heated with a 5% excess of ethyl p-toluenesulfonate at 140-145° for 6 hours. In the synthesis of the 3,3'-dimethyl derivatives the methyl-p-toluenesulfonates were obtained in similar manner, in in which connection the heating was done at 130-135°. Pyridine and the ortho ester of the carboxylic acid were added to the obtained quaternary salt, and the mixture was heated in an oil bath at 130-135° for 1 hour. Then the reaction mass was diluted with ether, the tarry precipitate dissolved in methyl alcohol, and the dye iodide isolated by the addition of aqueous potassium iodide solution. For purification the dyes were well washed with water and alcohol, after which they were recrystallized from ethyl alcohol until the melting point remained constant. Prior to analysis the dyes were dried *in vacuo* at 70-100° to constant weight.

The preparation conditions and yields of the dyes, their properties, and the analysis results, are all given in Table 2.

The absorption curves of the dyes were measured on a Koenig-Martens spectrophotometer in $1 \cdot 10^{-4}$ molar ethyl alcohol solutions.

SUMMARY

1. The 4,5- and 4,6-dimethoxy-2-methylbenzothiazoles were synthesized. From the quarternary salts of these compounds, and also from the earlier described 4,7- and 5,6-derivatives, were obtained a number of

4,5,4',5'-, 4,6,4',6'-, 4,7,4',7'- and 5,6,5',6'-tetramethoxythiacarbocyanines. The optical and photographic properties of these dyes were studied.

2. It was shown that in the transition from the dimethoxy- to the tetramethoxythiacarbocyanines a deepening of the color is observed for the 4,6,4',6'- 4,7,4',7'- and 5,6,5',6'-derivatives, while at the same time the absorption maximum for the 4,5,4',5'-tetramethoxy derivatives lies between the absorption maxima of the 4,4'- and 5,5'-dimethoxythiacarbocyanines.

3. The postulation was expressed that the heightened color of the 4,5,4',5'-tetramethoxythiacarbocyanines was associated with hindered electron reaction of the methoxy groups in these dyes with the polymethine chromophore due to spatial difficulties.

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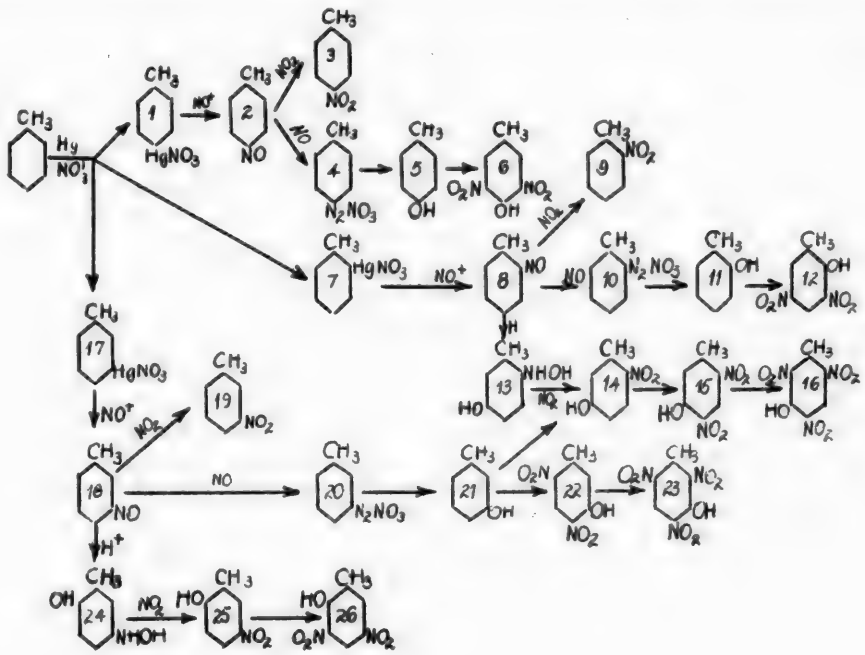
MECHANISM FOR THE CATALYTIC NITRATION OF AROMATIC COMPOUNDS IN THE PRESENCE OF MERCURY SALTS

III. NEW DIRECTIONS FOR THE REACTION IN THE NITRATION OF TOLUENE

A. I. Titov and A. N. Baryshnikova

The nitration of toluene with nitric acid in the presence of mercury was studied by Davis and coworkers [1], and also by Blechta and Patek [2]. From the nitration products they were able to isolate the nitrotoluenes, p-nitrobenzoic acid and trinitro-m-cresol. The main purpose of the present study was to show the application of our earlier developed theory [3] to finding new chemical phenomena in this reaction.

The main reaction courses in the catalytic nitration of toluene can be depicted by the following scheme:



The primary reaction products are the p-, o- and m-tolylmercury nitrates 1, 7 and 17, which under the influence of nitrogen dioxide are farther converted into the nitroso compounds 2, 8 and 18. The nitrosotoluene 2, as well as all of the nitroso compounds having substituents in the p-position to the nitroso group, under the influence of nitrogen dioxide are converted into p-nitrotoluene 3, while in the reaction with nitrogen oxide they are converted into p-toluenediazonium nitrate 4, which can be easily converted into p-cresol and then into dinitro-p-cresol 6.

The o-nitrosotoluene 8 and its m-isomer 18, originating in the same manner as the p-isomer, in addition to the indicated transformations into nitrotoluenes 9 and 19, diazo compounds 10 and 20 and normal nitrophenols 12 and 23, are also capable, under hydrogen-ion influence, of transition into the p-hydroxyhydroxylamines 13 and 24, which under the reaction conditions, in the final analysis, are converted into the anomalous nitrophenols 15, 16

and 26. The anomalous nitrophenols, in contrast to the normal analogs, have the hydroxyl group in the para-positions to the site occupied earlier by the nitroso group and mercury atom. We termed the simultaneous introduction of the nitro and hydroxyl groups as oxidative nitration [3].

The possibility and degree of conversion of the nitroso compounds by one or the other path depends on their structure, concentration of components in the equilibrium system $2HNO_3 + NO \rightleftharpoons 3NO_2 + H_2O$, and the temperature. In accord with earlier statements, the p-nitrosotoluene is practically incapable of conversion into the anomalous nitrophenols. The entrance of the o- and m-nitrosotoluenes into the oxidative nitration reaction is favored by an increase in acid concentration and by elevation of the temperature. It is natural for an increase in the nitrogen oxide concentration to facilitate the conversion of all of the nitrosotoluenes into diazo compounds, which are easily transformed at slightly elevated temperatures into the normal nitrophenols. A high nitrogen dioxide concentration should assure oxidation of the nitrosotoluenes to the nitrotoluenes.

The results for the experimental verification of the theoretical conclusions are given below.

With the oxidative nitration reaction representing a fairly high proportion of the total sum of the reactions, with only the o- and m-nitrosotoluenes entering into it, then in the mixture of formed nitrotoluenes the p-isomer should predominate. The validity of such a conclusion is well supported by our experimental data (cf. Experimental). In the first experiment a comparatively high nitric acid concentration facilitated oxidative nitration, and the amount of the p-isomer in the mixture of nitrotoluenes reached 62%, while in the usual mixture it is only 40%. In the second experiment the conversion of the o- and m-nitrosotoluenes into the anomalous nitrophenols was facilitated by temperature elevation, which also led to an increase in the amount of the p-isomer in the mixture of nitrotoluenes to 60.6%. The low amount of p-nitrotoluene in the mixture of nitro compounds from the third experiment (43%) is fully understandable. In this case the oxidative nitration reaction failed to possess decisive significance due to the low acid concentration and low temperature employed.

We were able to show the considerable formation of diazo compounds in the experiments on the catalytic nitration of toluene at low temperature and high nitric acid concentration, factors facilitating the retention of diazo compounds. Apparently, the decomposition of diazo compounds and its initiating action should be explained by the rapid course of the reaction between toluene and nitrogen dioxide in the presence of mercury nitrate, an observation that was made by us earlier [5].

From our theory it further follows that with a high nitrogen oxide content in the reaction sphere and with a low nitric acid strength that the relative proportion for the conversion of the nitrosotoluenes into the diazo compounds should increase, while the proportion for the oxidative nitration of the o- and m-nitroso compounds should decrease. If, under the experimental conditions, the diazo compounds are converted to the normal nitrophenols (cf. main scheme), then this should lead to a reduced amount of trinitro-m-cresol in the reaction product and to the appearance of considerable amounts of the dinitro derivatives of o- and p-cresol. Actually, we were able to show that under the conditions of constant saturation of the reaction mixture with nitrogen oxide that the main reaction product is dinitro-o-cresol, and, in addition, we established the formation of appreciable amounts of dinitro-p-cresol. By running the reaction under high nitrogen oxide pressure it is possible to unconditionally achieve even more impressive results.

The other data of our performed experiments are also found to be in agreement with the theory. Thus, for example, it can be stated that the relative yield of the nitrotoluenes was maximal in the first experiment due to the high amount of nitrogen dioxide present in the reaction sphere in the particular case, which dioxide functioned as an agent for the oxidation of the nitroso compounds to the nitro derivatives; the minimal yield proved to be in the second experiment due to shifting of the equilibrium $NO_2 + NO \rightleftharpoons N_2O_3$ to the right and suppression of the reaction for the oxidation of the nitrosotoluenes to the nitro derivatives due to transformation of the first to diazo compounds and their decomposition products.

The diversity of the chemical reactions in the catalytic nitration of toluene is far from being limited to the earlier examined directions. For example, the possibility should be mentioned of converting the nitrosotoluenes into the o- and p-dinitro derivatives, the nitrosoditolylhydroxylamines, etc. [3, 4]. It is also important to mention that due to the presence of nitrogen dioxide in the reaction sphere the paraffinic (alkyl) chain of toluene is drawn into reaction [6]. Thus, in the first experiment we were able to show the formation, besides p-nitrobenzoic acid, of benzyl nitrate and p-nitrobenzoate. In accord with our investigations [7], the source for the creation of p-nitrobenzoic acid is phenyldinitromethane, reacting in accord with the scheme:

$$C_6H_5CH(NO_2)_2 \xrightarrow{NO_2} C_6H_5C(NO_2)_3 \rightarrow p\text{-}NO_2C_6H_4\text{-}COOH,$$

while the formation of the phenylnitromethane and of benzyl alcohol and its esters was examined earlier [6].

To demonstrate the presence of benzyl p-nitrobenzoate in the reaction product we made use of its reaction with diethylamine, $p\text{-}NO_2\text{-}C_6H_4\text{-}COO\text{-}CH_2\text{-}C_6H_5 + NH(C_2H_5)_2 \rightarrow p\text{-}NO_2\text{-}C_6H_4\text{-}COOH + C_6H_5\text{-}CH_2\text{-}N(C_2H_5)_2$, to yield the free p-nitrobenzoic acid and benzyldiethylamine. The alkylation influence manifested by the ester, instead of an acylation action, as was determined (shown) by us earlier [8], is closely associated with the ease with which the benzyl group is converted into the benzyl cation and with the diminished electrophilic activity of the carboxylic carbon atom in acids of type Ar—COOH due to conjugation with the π-electrons of the nucleus.

EXPERIMENTAL

1. Oxidative Nitration of Toluene with Concentrated Nitric Acid at Around 5 to 10°. A mixture of 40 ml of toluene, 100 ml of nitric acid (d 1.32), 10 g of mercury nitrate and 2 g of sodium nitrate was allowed to stand in a one liter conical flask fitted with a ground-glass calcium chloride tube, filled with anhydrous calcium nitrate. After 10 days the acid layer was fortified with 40 ml of nitric acid (d 1.5) and 10 g of the mercury salt.

After 25 days of standing the reaction mass was cooled to 0°, filtered, and washed with 30 ml of cold toluene. From the precipitate 1.3 g of p-nitrobenzoic acid with m. p. 220-225° was isolated. Titration of the acid layer with β-naphthol showed the presence of about 1.3 g of mixed isomeric toluenediazonium nitrates. The organic layer was successively extracted with water, soda and alkali solutions, and then dried over potash. The soda extract was acidified, and the separated oil was steamdistilled. The residue in the distillation flask gave 1.84 g of trinitro-m-cresol with m. p. of about 90-100°, giving a higher melting point when heated with the pure product, and after recrystallization the trinitrocresol with m. p. 105°. Extraction of the distillate with ether gave 2.4 g of partially crystallized mixed nitrocresols. This mixture was treated with 1 ml of nitric acid (d 1.4) and 3 ml of H_2SO_4 at 100°; here the nitro derivatives of o- and p-cresol were decomposed. Dilution of this reaction mixture with water yielded 1.3 g of trinitro-m-cresol. Treatment of the alkaline extract in similar manner gave 0.52 g of nitrocresols, yielding 0.24 g of trinitro-m-cresol when treated with sulfuric acid-nitric acid mixture (mixed acid).

The toluene layer after drying was mixed with 10 ml of diethylamine and heated for 4 hours on the water bath in a flask under reflux, and then extracted with water and dilute hydrochloric acid. The presence of nitrate ion in the water extract was established; acidification yielded 0.12 g of p-nitrobenzoic acid. Alkalization of the acid extract yielded 0.31 g of benzyldiethylamine, identified as the picrate with m. p. 122° [8]. The residue from the preceding treatments was steam-distilled, the organic layer of the distillate dried, and then vacuum-distilled to yield 10.2 g of mixed nitrotoluenes with freezing point 25.5°, which corresponds to a 62% content of the p-isomer compared with 40% in the usual mixture. Without doubt the amount of p-isomer in the nitro product from this experiment was somewhat reduced due to the occurrence of parallel nitration through the nitronium cation.

2. Oxidative Nitration of Toluene with Dilute Nitric Acid Under Saturation with Nitrogen Oxide. A mixture of 50 ml of toluene, 200 ml of nitric acid (d 1.1) and 40 g of mercury nitrate was heated at 50-60° in a current of nitrogen oxide for 50 hours. The organic portion with stirring was successively extracted with water, 20 ml of 10% potassium bicarbonate solution, and 20 ml of soda solution. Acidification of the bicarbonate extract yielded 3.3 g of mixed nitrocresols, the treatment of which with 20 ml of 10% soda solution gave the Na salt of trinitro-m-cresol, from which 0.73 g of pure trinitro-m-cresol was obtained. Acidification of the mother liquor from the salts yielded 2.4 g of oil; its steam-distillate yielded dinitro-o-cresol with m. p. 83°, while the residual oil in the flask yielded 0.93 g of crystalline trinitro-m-cresol.

Acidification of the soda extract yielded 2.5 g of solid, which after recrystallization from alcohol gave 1.3 g of dinitro-o-cresol with m. p. ca. 83°, failing to show a melting point depression when mixed with the pure authentic product. Treatment of the alcohol mother liquor with 20 ml of 10% potash solution yielded 0.5 g of mixed potassium salts of the dinitro derivatives of o- and p-cresol. Recrystallization of the mixture from water gave 0.12 g of the bright red salt of dinitro-p-cresol, from which dinitro-p-cresol with m. p. 80-82° was isolated, failing to show a melting point depression when mixed with pure 2,6-dinitro-4-methylphenol. From the residue after the extraction with carbonate solutions the usual operations of drying and vacuum-distillation yielded 1.4 g of mixed nitrotoluenes with a freezing point of 7°.

3. Oxidative Nitration of Toluene with Dilute Nitric Acid at 100° Without Nitrogen Oxide Saturation. A mixture of 20 ml of toluene, 100 ml of nitric acid (d 1.1), 20 g of mercury nitrate and 0.2 g of trioxymethylene was heated for 10 hours on the boiling water bath in a flask under reflux. Treatment of the reaction mixture in the same manner as just described yielded 2.19 g of trinitro-m-cresol, 0.15 g of dinitro-o-cresol, 0.8 g of mixed nitrocresols, 2.3 g of mixed nitrotoluenes with freezing point 24.5°, and 7.6 g of insoluble mercury salts and polyorganomercury compounds.

4. Alkylation with the Benzyl Esters of Benzoid and p-Nitrobenzoid Acid. A mixture of 1 g of benzyl p-nitrobenzoate, 5 ml of nitrobenzene and 3 ml of diethylamine was heated for 8 hours on the water bath in a small flask under reflux, after which it was successively treated with water and dilute hydrochloric acid, and then steam-distilled. The water extract yielded 0.12 g of p-nitrobenzoic acid. Treatment of the acid extract in the usual manner yielded 0.15 g of benzyldiethylamine, identified as the picrate and from its mixed melting point with the authentic product. The residue from the steam-distillation yielded 0.73 g of the p-nitrobenzoate with m. p. around 80°. We were able to show that alkylation also took place in a similar experiment with benzyl benzoate.

SUMMARY

1. In accord with the theory for the reaction it was found that in the catalytic nitration of toluene the following holds:

a) the mixture of nitrotoluenes can have a high content of the para-isomer;

b) toluenediazonium salts are formed;

c) when dilute nitric acid is used and the reaction mixture is saturated with nitrogen oxide, the main reaction product is dinitro-o-cresol with the concurrent formation of the nitro derivatives of m- and p-cresol;

d) the yield of nitrotoluenes is increased with increase in the nitrogen dioxide concentration.

2. The presence of benzyl p-nitrobenzoate and benzyl nitrate in the reaction product was shown and the mechanisms for their formation were indicated.

3. The benzyl esters of the aromatic acids of type Ar—COOH function as alkylation agents in the reaction with diethylamine.

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ACTION OF ALKYL IODIDES ON ESTERS OF PHENYLALKYLARSENIOUS ACIDS

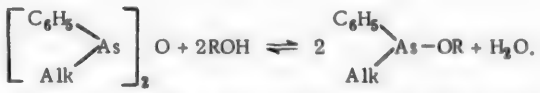
I. M. Starshov and Gilm Kamai

In previous communications one of us [1, 2] had shown that the esters of the arsenious acids: $As(OR)_3$, $ArAs(OR)_2$ and Ar_2AsOR, in constrast to the analogous esters of phosphorous and the arylphosphinic acids, under the influence of alkyl halides in the conditions of the Arbuzov rearrangement [3], fail to be isomerized into pentavalent arsenic compounds. It was also established that the cuprous halides react to form crystalline addition products with only those esters of arsenious acid as more closely resemble the arsines in their properties.

The mixed cyclic esters of arsenious acid also fail to react with alkyl iodides and with cuprous halides [4].

In the present communication we describe the results obtained when we studied the reaction of cuprous chloride and of alkyl halides with a number of phenylalkylarsenious acid esters.

Our starting substances were the alkyl iodides (where R = CH_3, C_2H_5, n-C_3H_7 and n-C_4H_9) and the esters that were obtained in the reaction of the corresponding alcohols with bis(phenylalkylarsine) oxides in accord with the equation:

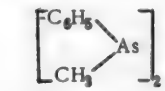
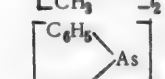
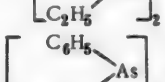
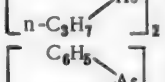


The reaction of alcohols with the oxides of secondary aralkyl arsines under conditions approximating those used for the esterification of arsenious anhydride [5] and phenylarsine oxide (arsenosobenzene) [6] with alcohols was realized for the first time in this study.

In this way we prepared the methyl, ethyl, n-propyl and n-butyl esters of phenylmethyl-, phenylethyl-, phenyl-n-propyl- and phenyl-n-butylarsenious acids. These esters, as derivatives of trivalent arsenic, lie close to the arsines in their properties, and easily add the cuprous halides, as well as the alkyl bromides and iodides.

The alkyl iodide addition products of the esters – the phenyldialkylalkoxyarsonium iodides – are colorless crystalline substances.

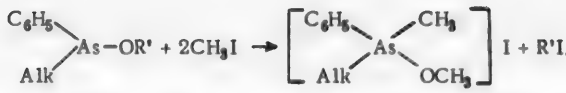
TABLE 1

Formula	Boiling point	d_0^{20}	n_D^{20}	MR	$AR_{As}^{=}$	% As		Yield (in %)
				Found	Found	Found	Calculated	
	154-155° (3 mm)	1.4381	1.6252	86.09	11.30	42.48	42.88	75.5
	191-192 (9 mm)	1.3564	1.6062	96.17	11.72	39.41	39.64	85.0
	214-215 (10 mm)	1.2925	1.5900	106.02	12.03	36.58	36.89	90.0
	231-232 (18 mm)	1.2460	1.5746	115.10	11.95	34.27	34.57	95.0

The reaction of methyl iodide with the n-propyl and n-butyl esters of phenylmethylarsenious acid, and also with some of the other phenylalkylarsenious acid esters, is more complex and proceeds with profound change as shown in the scheme:

TABLE 2

Formula of the ester	Boiling point	Pressure (in mm)	d_4^{20}	n_D^{20}	AR_{As}^{m}	Amount of As (in %)		Yield (in %)
						Found	Calculated	
C_6H_5, CH_3, As–OCH_3	95-96°	17	1.2975	1.5628	11.27	37.76	37.82	24.0
C_6H_5, CH_3, As–OC_2H_5	102-103	20	1.2473	1.5559	11.75	35.36	35.33	33.0
C_6H_5, CH_3, As–OC_3H_7-n	114-114.5	18	1.1987	1.5403	11.70	33.05	33.14	63.0
C_6H_5, CH_3, As–OC_4H_9-n	122-123	18	1.1675	1.5338	11.78	31.23	31.19	85.6
C_6H_5, C_2H_5, As–OCH_3	92-93	10	–	–	–	35.04	35.33	20.0
C_6H_5, C_2H_5, As–OC_2H_5	105-106	12	1.1980	1.5430	11.93	33.37	33.14	35.0
C_6H_5, C_2H_5, As–OC_3H_7-n	110-111	10	1.1692	1.5345	11.76	31.03	31.19	61.5
C_6H_5, C_2H_5, As–OC_4H_9-n	122-123	10	1.1448	1.5295	11.77	29.50	29.48	79.0
C_6H_5, n-C_3H_7, As–OCH_3	102-103	10	–	–	–	32.65	33.14	26.0
C_6H_5, n-C_3H_7, As–OC_2H_5	101-103	7	1.1700	1.5360	11.86	31.49	31.19	30.0
C_6H_5, n-C_3H_7, As–OC_3H_7-n	126.5-127	12.5	1.1397	1.5280	11.93	29.56	29.48	81.5
C_6H_5, n-C_3H_7, As–OC_4H_9-n	120-121	4	1.1253	1.5260	11.80	28.05	27.94	85.0
C_6H_5, n-C_4H_9, As–OCH_3	117-118	12	1.1747	1.5380	11.81	31.04	31.19	31.0
C_6H_5, n-C_4H_9, As–OC_2H_5	127-128	12	1.1454	1.5318	11.98	29.71	29.48	38.0
C_6H_5, n-C_4H_9, As–OC_3H_7-n	139-140	10	1.1158	1.5220	11.93	27.77	27.94	68.0
C_6H_5, n-C_4H_9, As–OC_4H_9-n	154-155	16.5	1.1038	1.5198	11.73	26.55	26.56	80.0



In addition to the addition products shown in Table 3, we isolated colorless crystalline substances from the reaction of ethyl iodide, n-propyl iodide or n-butyl iodide with the n-butyl esters of phenylmethyl-, phenyl-n-propyl- or phenyl-n-butylarsenious acid, which substances were not studied in more detail by us.

EXPERIMENTAL

The starting substance – phenyldichloroarsine – was prepared by the method of Sherlin and Bras [8]. Based on phenylhydrazine the product yield was 64%.

The bis(phenylalkylarsine) oxides needed for the synthesis of the phenylalkylarsenious acid esters were prepared by the method described earlier by one of us [7]; some of the data for these oxides are given in Table 1.

Preparation of Methyl Phenylmethylarsenite

In a flask with cap, filled with anhydrous copper sulfate, and reflux condenser was placed 33 g of bis(phenylmethylarsine) oxide and 18 ml of methyl alcohol. The flask contents were heated in a metal bath for 3 hours at 100-120°. After cooling the reaction mixture was transferred to an Arbuzov distillation flask.

Vacuum-distillation of the mixture gave two fractions: 1st with b. p. 91-103° (16 mm); 2nd with b. p. 154-156° (3 mm). Redistillation of the 1st fraction gave a substance with b. p. 95-96° at 17 mm.

Found %: As 37.76. $C_8H_{11}OAs$. Calculated %: As 37.82.

The isolated methyl ester of phenylmethylarsenious acid is a colorless liquid; the yield of pure ester was 24%.

d_0^{20} 1.2975, n_D^{20} 1.5628.

The fraction with b. p. 154-156° was unreacted bis(phenylmethylarsine) oxide.

Other esters of the phenylalkylarsenious acids were obtained by the described method, starting from the corresponding alcohols and bis(phenylalkylarsine) oxides.

The isolated esters are colorless liquids. They are readily soluble in acetone, ether, alcohol, dichloroethane and other organic solvents. Many of them have a sharp odor, irritating the mucous membrane of the nose and eyes. The obtained esters are characterized in Table 2.

Preparation of $C_6H_5(CH_3)As{-}OCH_3 \cdot CuCl$. A mixture of 1.5 g of methyl phenylmethylarsenite with 0.8 g of cuprous chloride was prepared. The reaction proceeded with self-heating. The mixture crystallized on cooling. The crystals are soluble in hot benzene. After filtration the addition product was precipitated from benzene with ethyl ether. M. p. 70-72°.

Found %: Cl 11.45. $C_8H_{11}OAs \cdot CuCl$. Calculated %: Cl 11.93.

Preparation of $C_6H_5(C_4H_9)As{-}OCH_3 \cdot CuCl$. A mixture of 1.5 g of the ester and 0.8 g of cuprous chloride was heated for 2 hours at 60°. The flask contents crystallized on cooling. After recrystallization from ethyl alcohol the substance melted at 40-41°. Greenish crystals, soluble in benzene, ether and alcohol.

Found %: Cl 10.09. $C_{11}H_{17}OAs \cdot CuCl$. Calculated %: Cl 10.45.

Addition of Methyl Iodide to Methyl Phenylmethylarsenite

A mixture of 7.5 g of methyl phenylmethylarsenite and 5.4 g of methyl iodide was sealed in a tube from which the air had been displaced by carbon dioxide (gas). The tube was allowed to stand at 19-20° for 60 hours. After several hours a slight contraction of the liquid volume could be detected and the appearance of crystals. The crystals, precipitated with ether from acetone, had m. p. 108-109°.

Found %: As 22.28; I 37.21. $C_9H_{14}OAsI$. Calculated %: As 22.08; I 37.29.

The addition product – phenyldimethylmethoxyarsonium iodide – is obtained as colorless crystals, soluble in water, alcohol, dichloroethane and acetone.

TABLE 3

Starting products	Reaction Temperature	Ratio of Reactants	Time) (in hrs)	Formula of obtained product	Melting point	% As		% I	
						Found	Calculated	Found	Calculated
C_6H_5, CH_3 As–OCH_3 + CH_3I	19-20°	1 : 1	60	C_6H_5, OCH_3, $(CH_3)_2$ As I	108-109°	22.28	22.08	37.21	37.29
C_6H_5, CH_3 As–OC_3H_7 + CH_3I	20	1 : 1	120	C_6H_5, OCH_3, $(CH_3)_2$ As I	109-110	22.42	22.08	37.32	37.29
C_6H_5, CH_3 As–OC_4H_9 + CH_3I	40	1 : 1.8	10	C_6H_5, OCH_3, $(CH_3)_2$ As I	109-110	22.37	22.08	37.39	37.29
C_6H_5, C_2H_5 As–OC_2H_5 + C_2H_5I	100	1 : 1	8	C_6H_5, OC_2H_5, $(C_2H_5)_2$ As I	111-113	19.72	19.61	33.21	33.17
C_6H_5, C_2H_5 As–OC_3H_7 + CH_3I	20-30	1 : 2	120	C_6H_5, C_2H_5, OCH_3, CH_3 As I	112-114	21.12	21.15	35.63	35.81
C_6H_5, n-C_3H_7 As–OC_3H_7 + C_3H_7I	140	1 : 1	5	C_6H_5, OC_3H_7, $(C_3H_7)_2$ As I	162-163	17.45	17.66	30.27	29.91
C_6H_5, n-C_4H_9 As–OC_4H_9 + C_4H_9I	130-150	1 : 1	16	C_6H_5, OC_4H_9, $(C_4H_9)_2$ As I	135-136	16.13	16.07	27.63	27.20
C_6H_5, n-C_4H_9 As–OC_4H_9 + CH_3I	20	1 : 1	5	C_6H_5, OC_4H_9, C_4H_9, CH_3 As I	139-141	17.97	17.66	30.40	29.91

Reaction of Methyl Iodide with n-Propyl Phenylmethylarsenite

A mixture of 8.1 g of n-propyl phenylmethylarsenite and 5 g of methyl iodide was sealed in a tube. The tube was allowed to stand at room temperature for 120 hours. The tube contents partially crystallized. The addition product was purified by its precipitation from acetone solution with anhydrous ether. M. p. 109-110°.

Found %: As 22.42; I 37.32. C_9H_{14} OAsI. Calculated %: As 22.08; I 37.29.

From the analysis data the obtained substance is phenyldimethylmethoxyarsonium iodide.

The reaction of other alkyl iodides with the esters of the phenylalkylarsenious acids was run in the same manner as described above. The data for the obtained substances are given in Table 3.

SUMMARY

1. It was shown that the reaction of alcohols with bis (phenylalkylarsine) oxides yields the corresponding phenylalkylarsenious acid esters in good yields. Sixteen new esters were synthesized by this method.

2. The reaction of cuprous chloride and of alkyl iodides with the esters of the phenylalkylarsenious acids was studied. The synthesis of 6 new arsonium salts is described.

3. It was established that the reaction of methyl iodide with the n-propyl and n-butyl esters of phenylmethylarsenious acid is quite complex and leads to the formation of phenyldimethylmethoxyarsonium iodide.

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* T. p. = C. B. Translation pagination.

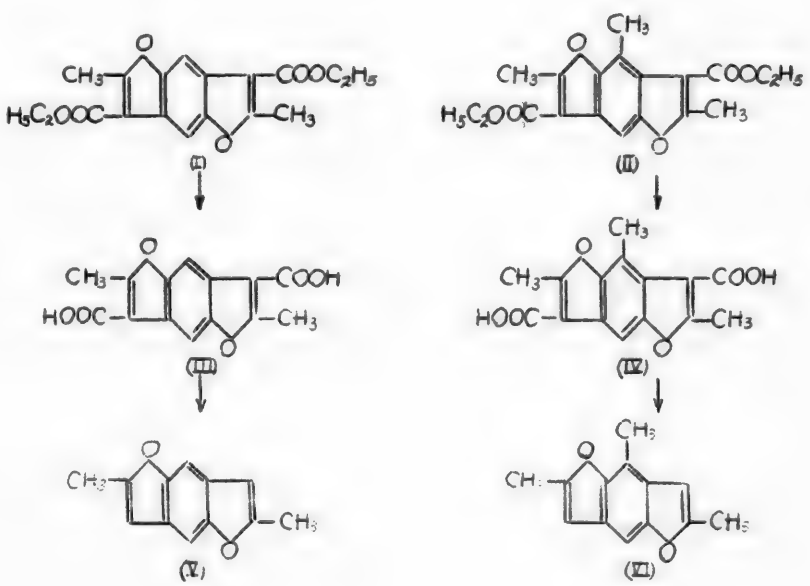
QUINONES

III. SYNTHESIS OF SUBSTITUTED BENZODIFURANS BY THE REACTION OF p-BENZOQUINONE AND TOLUQUINONE WITH ACETOACETIC ESTER

A. P. Terentyev, A. N. Grinev, and Pan Bon-Khvar

von Pechmann [1] was the first to establish that the reaction between p-benzoquinone and acetoacetic ester, in the presence of zinc chloride, leads to the formation of two crystalline compounds with m. p. 137 and 184°, corresponding to the empirical formulas $C_{12}H_{12}O_4$ and $C_{18}H_{18}O_6$. Later [2, 3] a scheme for this reaction was given, structural formulas for the substances obtained by von Pechmann were proposed, and the condensation of toluquinone with acetoacetic ester was also run. It was found that the yield of one of the substances obtained by von Pechmann, the benzofuran derivative, reaches 50% [2]. The yield of the other substance, the benzodifuran derivative, was not shown.

We selected such conditions for running the reaction as would predominantly give benzodifuran derivatives, and some of their transformations were realized. The condensation of p-benzoquinine and of toluquinone with acetoacetic ester gave the diethyl ester of 2,6-dimethylbenzo[1,2,-b, 4,5-b'] difuran-3,7-dicarboxylic acid (I) (yield 70%, based on the quinone) and the diethyl ester of 2,4,6-trimethylbenzo [1,2-b, 4,5-b'] difuran-3,7-dicarboxylic acid (II) (yield 60%), respectively. Saponification of the esters gave the earlier described [1,3] dibasic acids (III and IV), which under decarboxylation by heating with quinoline and copper oxide gave the previously unknown 2,6-dimethylbenzo[1,2-b, 4,5-b'] difuran (V) and 2,4,6-trimethylbenzo[1,2-b, 4,5-b'] difuran (VI) in good yields.



EXPERIMENTAL

Condensation of p-Benzoquinone with Acetoacetic Ester. To a solution of zinc chloride (28 g, 0.2 mole) in 28 g of anhydrous alcohol was added 39 g (0.3 mole) of the ester, and then with heating and stirring in 3-4 portions (over 5-10 minutes) was added 21 g (0.2 mole of p-benzoquinone. The flask contents were heated on the boiling water bath with constant stirring for 45 minutes, and then allowed to stand at room temperature for several hours. The obtained crystalline mass was separated and washed with a little ether. The crystalline benzodifuran derivative (I) had m. p. 184° (from a 1:1 mixture of dichloroethane and acetone). The yield of pure substance was 20.4 g (70%, based on p-benzoquinone). The mother liquor was diluted with water and allowed to stand for several hours. The water was decanted from the viscous semicrystalline precipitate and the precipitate was dissolved in ether. The ether extract was washed with water, then dried over calcium chloride, and evaporated. The obtained crystals were recrystallized from benzene. There was obtained 4.5 g of the benzofuran derivative with m. p. 137°, which melting point agrees with the literature [2]. The ester (I) was saponified with alcoholic caustic. The obtained sodium salt precipitate of the acid (III) was dissolved in water. Acidification with hydrochloric acid (to Congo) gave the acid (III).

Preparation of 2,6-Dimethylbenzo[1,2-b, 4,5-b']difuran (V). A mixture of 2 g of the acid (III), 4.5 g of quinoline and 0.1 g of copper oxide was heated for 2 hours at 240-242° in a distillation flask. Then the temperature was raised and the flask contents were distilled. The distillate was acidified with dilute hydrochloric acid to acid reaction. The resulting crystals were filtered, and then purified by steam-distillation and one recrystallization from alcohol. The product (V) was obtained as white crystals with m. p. 113-114° and having a pleasant odor. The yield of the purified substance was 1.2 g.

Found %: C 77.22, 77.42; H 5.63, 5.65. $C_{12}H_{10}O_2$. Calculated %: C 77.40; H 5.41.

Condensation of Toluquinone with Acetoacetic Ester. The reaction was run the same as for p-benzoquinone. For reaction was taken 5 g (0.04 mole) of toluquinone, 6.5 g (0.05 mole) of acetoacetic ester, 5.5 g (0.04 mole) of zinc chloride and 5.5 g of anhydrous alcohol. The crystals obtained for the reaction were separated and recrystallized from a mixture of acetone and dichloroethane. The yield of purified benzodifuran derivative (II) was 3.2 g (60%, based on the quinone), m. p. 120-122°.

From the mother liquor was isolated 1 g of the benzofuran derivative with m. p. 173°, which melting point agrees with the literature [3]. Saponification of the ester (II) as before gave the acid (IV).

Preparation of 2,4,6-Trimethylbenzo[1,2-b, 4,5-b']difuran (VI). For reaction was taken: acid (IV) 0.7 g, quinoline 2 g, copper oxide 0.1 g. The product (VI) was obtained as white crystals with m. p. 70-71.5° (from alcohol). Yield of purified substance 0.3 g.

Found %: C 77.83, 77.89; H 6.20, 6.03. $C_{13}H_{12}O_2$. Calculated %: C 77.98; H 6.05.

SUMMARY

A method was developed for the preparation of the diethyl esters of 2,6-dimethyl- and 2,4,6-trimethylbenzo[1,2-b, 4,5-b']-difuran-3,7-dicarboxylic acids. Saponification of the esters yielded dibasic acids, the decarboxylation of which gave the 2,6-dimethyl- and 2,4,6-trimethylbenzo[1,2-b, 4,5-b']difurans.

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SYNTHESIS OF p-HYDROXYBENZENESULFONIC ACID DERIVATIVES

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The purpose of the present work was to synthesis the hydrazides of p-hydroxy- and p-ethoxybenzenesulfonic acids and a number of their derivatives, and also the derivatives of these acids with the complex-forming amines – ethylenediamine and phenylenediamine.

Usually the hydrazides of carboxylic acids are obtained by reacting either the esters or amides of the acids with hydrazine hydrate, but this method is not applicable to the preparation of the hydrazides of either p-hydroxy- or p-ethoxybenzenesulfonic acid. The esters of these acids are easily hydrolyzed in the presence of hydrazine hydrate and form hydrazine salts of the sulfonic acid. The amide group of sulfonic acids is not substituted by the hydrazide group even when heated in a sealed tube [1]; consequently, we obtained the hydrazides of p-hydroxy- and p-ethoxybenzenesulfonic acids by the reaction of the acid chlorides of these acids [2, 3] with hydrazine hydrate.

This reaction proceeds with good yield in aqueous medium; in nonaqueous solvents (alcohol, benzene, dioxane) the hydrazides are obtained in very low yields. The reaction of aqueous or alcoholic solutions of the hydrazides of p-hydroxy or p-ethaxybenzenesulfonic acid with aldehydes gave well-crystallized hydrazones.

The condensation of the acid chlorides of p-benzoyloxybenzenesulfonic acid or p-ethoxybenzenesulfonic acid with p-acetaminoaniline (4'-aminoacetanilide) in the presence of soda, followed by saponification of the reaction products with aqueous sodium hydroxide solution, gave p-hydroxy-p'-aminobenzenesulfonamilide and p-ethoxy-p'-aminobenzenesulfonanilide, respectively [4]. p-Bis(p-ethoxybenzenesulfonamido) benzene was obtained in the attempts made to condense p-ethoxybenzenesulfonyl chloride with p-phenylenediamine.

The condensation of p-benzoyloxybenzenesulfonyl chloride and p-ethoxybenzenesulfonyl chloride with aqueous solutions of N-acetylethylenediamine in the presence of soda [5] was used to prepare N-(β-aminoethyl)-p-hydroxy- and N-(β-aminoethyl)-p-ethoxybenzenesulfonamide, respectively.

As was revealed, the acid chlorides of these acids react very slowly with N-acetylethylenediamine in the absence of solvent, while in benzene solution the reaction proceeds quite rapidly. The final reaction products lend themselves to purification with difficulty.

All of the compounds synthesized by us were tested for their bactericidal action. The testing revealed that not one of them possessed significant antitubercular activity.

EXPERIMENTAL

p-Hydroxybenzenesulfonic Acid Hydrazide. To a solution of 5 g of hydrate in 5 ml of water was gradually added 10 g of p-benzoyloxybenzenesulfonyl chloride; here the temperature of the reaction mass was raised to 90°. Then the mixture was cooled, and the separated crystalline substance was filtered and recrystallized from water. Yield 4.5 g (71%); m. p. 160-165° (decompn.) After recrystallization from alcohol the hydrazide of p-hydroxybenzenesulfonic acid was obtained as a white crystalline powder with m. p. 165-166° (decompn.), readily soluble in acids, water, and the usual organic solvents.

3.735 mg sub.: 5.200 mg CO_2; 1.487 mg H_2O. Found %: C 37.99; H 4.45. $C_6H_8O_3N_2S$. Calculated %: C 38.29; H 4.28.

p-Hydroxybenzenesulfonic Acid (p-Hydroxybenzylidene) hydrazide. To a boiling solution of 1 g of the hydrazide of p-hydroxybenzenesulfonic acid in 20 ml of water was added a boiling solution of 0.65 g of p-hydroxybenzaldehyde in 5 ml of water. The reaction mass was cooled after boiling for 5 minutes, and the crystallized substance was filtered and recrystallized twice from aqueous alcohol.

The (p-hydroxybenzylidene)hydrazide of p-hydroxybenzene-sulfonic acid is a yellow crystalline powder with m. p. 148-149°, readily soluble in alcohol, acetone and ethyl acetate, and insoluble in benzene, ether and chloroform.

4.428 mg sub.: 8.100 mg CO_2; 1.750 mg H_2O. Found %: C 49.92; H 4.42. $C_{13}H_{12}O_4N_2S \cdot H_2O$. Calculated %: C 50.31; H 4.54. After drying over P_2O_5: 3.318 mg sub.: 6.432 mg CO_2; 1.178 mg H_2O. Found %: C 52.90; H 3.97; $C_{13}H_{12}O_4N_2S$. Calculated: C 53.44; H 4.13.

p-Hydroxybenzenesulfonic Acid (p-Acetaminobenzylidene)hydrazide. To a hot solution of 1 g of the hydrazide of p-hydroxybenzenesulfonic acid in 20 ml of water was added a solution of 0.9 g of p-acetaminobenzaldehyde in 15 ml of water. The mixture was heated at the boil for 5 minutes, and the substance crystallized on cooling. After two recrystallizations from aqueous alcohol the (p-acetaminobenzylidene)hydrazide of p-hydroxybenzenesulfonic acid was obtained as an orange crystalline powder with m. p. 184-185° (decompn.), readily soluble in alcohol, acetone and ethyl acetate, and poorly soluble in benzene and ether.

4.409 mg sub.: 8.711 mg CO_2; 1.960 mg H_2O. Found %: C 53.91; H 4.97. $C_{15}H_{15}O_4N_3S$. Calculated %: C 54.04; H 4.53.

P-Hydroxybenzenesulfonic Acid (p-Dimethylaminobenzylidene)hydrazide. To a hot solution of 1 g of the hydrazide of p-hydroxybenzenesulfonic acid in 30 ml of anhydrous alcohol was added 0.8 g of p-dimethylaminobenzaldehyde and the mixture was boiled for 5 minutes. After long cooling a grayish-green substance crystallized. After two recrystallizations from 25% acetic acid the (p-dimethylaminobenzylidene)hydrazide of p-hydroxybenzenesulfonic acid was obtained as a pinkish crystalline substance with m. p. 157-158° (decompn.), readily soluble in alcohol, acetone and chloroform.

3.431 mg sub.: 7.101 mg CO_2; 1.660 mg H_2O. Found %: C 56.48; H 5.41. $C_{15}H_{17}O_3N_3S$. Calculated %: C 56.42; H 5.36.

p-Ethoxybenzenesulfonic acid Hydrazide. To a solution of 10 g of hydrazine hydrate in 10 ml of water was gradually added 20 g of p-ethoxybenzenesulfonyl chloride. On conclusion of addition the hot reaction mass was cooled, the crystallized substance filtered, washed with ice water, and recrystallized from water. There was obtained 15 g (76%) of the hydrazide of p-ethoxysulfonic acid with m. p. 109-111° (decompn). Recrystallization from anhydrous alcohol gave white lustrous needles with m. p. 111° (decompn.), readily soluble in the ordinary organic solvents.

8.800 mg sub.: 1.025 ml N_2 (25°, 731 mm). Found %: N 12.83. $C_8H_{12}O_3N_2S$. Calculated %: N 12.95.

p-Ethoxybenzenesulfonic Acid (p-Acetaminobenzylidene)hydrazide. To a hot solution of 2 g of the hydrazide of p-ethoxybenzenesulfonic acid in 40 ml of water was added a solution of 1.35 g of p-acetaminobenzaldehyde in 25 ml of water, and the mixture was boiled for 5 minutes. Then the solution was cooled; the separated crystalline substance was filtered and then recrystallized twice from alcohol. The (p-acetaminobenzylidene)hydrazide of p-ethoxybenzenesulfonic acid was obtained as a white crystalline powder with m. p. 186-186.5° (decompn.), readily soluble in acetone and acetic acid, and insoluble in dichloroethane and chloroform.

3.673 mg sub.: 7.642 mg CO_2; 1.750 mg H_2O. Found %: C 56.78; H 5.33. $C_{17}H_{19}O_4N_3S$. Calculated %: C 56.49; H 5.29.

p-Ethoxybenzenesulfonic Acid (p-Dimethylaminobenzylidene)-hydrazide. To a hot solution of 2 g of the hydrazide of p-ethoxybenzenesulfonic acid in 10 ml of anhydrous alcohol was added 1.6 g of p-dimethylaminobenzeldehyde. The (p-dimethylaminobenzylidene)hydrazide of p-ethoxybenzenesulfonic acid that separated on standing was recrystallized from alcohol to give a white crystalline powder with 170-171° (decompn.), soluble in acetone, alcohol, acetic acid, chloroform and dichloroethane.

3.590 mg sub.: 7.738 mg CO_2; 1.969 mg H_2O. Found %: C 58.82; H 6.13. $C_{17}H_{21}O_3N_3S$. Calculated %: C 58.76; H 6.09.

p-Ethoxybenzenesulfonic Acid (4-Hydroxy-3-methoxybenzylidene)hydrazide. To a hot solution of 2 g of the hydrazide of p-ethoxybenzenesulfonic acid in 40 ml of water was added a solution of 1.7 g of vanillin in 35 ml of water, and the mixture was boiled for 5 minutes. The separated oily substance solidified on standing.

The (4-hydroxy-3-methoxybenzylidene)hydrazide of p-ethoxybenzenesulfonic acid was recrystallized twice from dilute acetic acid to give a white crystalline powder with m. p. 128-130° (decompn.), readily soluble in alcohol, acetone and chloroform.

3.524 mg sub.: 7.124 mg CO_2; 1.572 mg H_2O. Found %: C 55.17; H 4.99. $C_{16}H_{18}O_5N_2S$. Calculated %: C 54.84; H 5.17.

p-Ethoxy-p'-aminobenzenesulfonanilide. A mixture of 16 g of p-acetaminoaniline, 24 g of p-ethoxybenzenesulfonyl chloride, 17 g of soda and 80 ml of water was stirred at room temperature for 6 hours, after which it was heated at 40° for 1 hour. The resulting p-ethoxy-p'-acetaminobenzenesulfonanilide was filtered, washed with water, and saponified by boiling with 100 ml of 20% aqueous sodium hydroxide solution for 2 hours. Then the solution was diluted with an equal volume of water and acidified with acetic acid. The separated p-ethoxy-p'-aminobenzenesulfonanilide was dissolved with heating in 250 ml of water made acid with hydrochloric acid, decolorized, and made alkaline with saturated sodium bicarbonate solution. The p-ethoxy-p'-aminobenzenesulfonanilide was obtained as a whitish crystalline powder with m. p. 155-156°, soluble in alcohol, chloroform and acetone.

3.280 mg sub.: 6.941 mg CO_2; 1.587 mg H_2O. Found %: C 57.75; H 5.41. $C_{14}H_{16}O_3N_2S$. Calculated %: C 57.52; H 5.51.

p-Hydroxy-p'-aminobenzenesulfonanilide. A mixture of 10 g of p-acetaminoaniline, 19.4 g of p-benzoyloxybenzenesulfonyl chloride, 10 g of soda and 50 ml of water was stirred at room temperature for 5 hours. On conclusion of reaction the precipitate was filtered, washed with water, and saponified by boiling with 150 ml of 20% aqueous sodium hydroxide solution for 2 hours. Then the solution was acidified with acetic acid. The separated p-hydroxy-p'-aminobenzenesulfonanilide was dissolved with heating in 100 ml of water made acid with hydrochloric acid, decolorized, and then made alkaline with saturated sodium bicarbonate solution. After two recrystallizations from water the p-hydroxy-p'-aminobenzenesulfonanilide was obtained as a whitish crystalline powder with m. p. 200-201°, soluble in alcohol and acetone, and insoluble in ether and chloroform.

3.959 mg sub.: 7.945 mg CO_2; 1.662 mg H_2O. Found %: C 54.77; H 4.69. $C_{12}H_{12}O_3N_2S$. Calculated %: C 54.53; H 4.58.

p-Bis(p-ethoxybenzenesulfonamido)benzene. To a solution of 15 g of phenylenediamine in 50 ml of water was added 9 g of p-ethoxybenzenesulfonyl chloride, and the mixture was stirred for 2.5 hours at 45°. Then the reaction mass was made alkaline, the separated phenylenediamine removed, and from the alkaline solution after acidification a substance, difficultly soluble in the ordinary organic solvents, was isolated. After recrystallization from glacial acetic acid and then from nitrobenzene the substance was obtained as a fine crystalline violet powder with m. p. 246° (decompn).

3.701 mg sub.: 7.519 mg CO_2; 1.721 mg H_2O. Found %: C 55.44; H 5.20 $C_{22}H_{24}O_6N_2S_2$. Calculated %: C 55.44; H 5.10.

N-(β-Aminoethyl)-p-hydroxybenzenesulfonamide. To a solution of 3.75 g of N-acetylethylenediamine and 4.5 g of soda in 50 ml of water was added a solution of 12 g of p-benzoyloxybenzenesulfonyl chloride in 50 ml of benzene, and the mixture was stirred at 50° for 3 hours. Then the benzene and part of the water was distilled off, and the obtained precipitate filtered and washed with water. The substance was saponified by boiling with 60 ml of 20% aqueous hydrochloric acid solution for 26 hours. On conclusion of reaction the benzoic acid was removed, the filtrate evaporated *in vacuo*, and the residue recrystallized thrice from concentrated hydrochloric acid. A white crystalline powder with m. p. 240-243° (decompn.) was obtained, readily soluble in water, and poorly soluble in alcohol.

15.565 mg sub.: 1.5 ml N_2 (25°, 757 mm). 9.120 mg sub.: 1.82 ml 0.02 N $AgNO_3$. Found %: N 10.98; Cl 14.15. $C_8H_{12}O_3N_2S \cdot HCl$. Calculated %: N 11.08; Cl 14.02.

N-(β-Aminoethyl)-p-ethoxybenzenesulfonamide. To a solution of 3.75 g of N-acetylethylenediamine and 4.5 g of soda in 50 ml of water was added a solution of 9 g of p-ethoxybenzenesulfonyl chloride in 50 ml of benzene. The mixture was heated at 50° for 3.5 hours. The substance obtained after distilling off the benzene was separated, washed with water, and saponified by boiling with 45 ml of 20% aqueous hydrochloric acid solution for 26 hours. On conclusion of reaction the solution was evaporated, and the residue was recrystallized twice from anhydrous alcohol and then from concentrated hydrochloric acid. White crystalline powder with m. p. 236° (decompn.), readily soluble in water, and moderately soluble in alcohol.

33.733 mg sub.: 6.16 ml 0.02 N $AgNO_3$. 4.506 mg sub.: 0.400 ml N_2 (19°, 734 mm). Found %: Cl 12.95; N 10.02. $C_{10}H_{16}O_3N_2S \cdot HCl$. Calculated %: Cl 12.63; N 9.97.

SUMMARY

The following were synthesized: 1) the hydrazide of p-hydroxybenzenesulfonic acid and from it the corresponding hydrazones with p-hydroxybenzaldehyde, p-acetaminobenzaldehyde, and p-dimethylaminobenzaldehyde; 2) the hydrazide of p-ethoxybenzenesulfonic acid and from it the corresponding hydrazones with p-acetaminobenzaldehyde, p-dimethylaminobenzaldehyde and vanillin; 3) the p-aminoanilides of p-ethoxy- or p-hydroxybenzenesulfonic acid and p-bis(p-ethoxybenzenesulfonamido)benzene; 4) N-(β-aminoethyl)-p-hydroxybenzenesulfonamide and N-(β-aminoethyl)-p-ethoxybenzenesulfonamide.

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PREPARATION OF TRIMETHYLFURFURYLAMMONIUM SALTS

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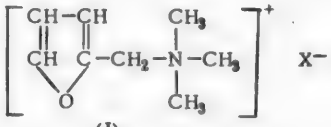
Some of the salts of quaternary ammonium bases, containing the furan or tetrahydrofuran ring, are used as medicinals [1]. At the present time the trimethylfurfuryl ammonium salts (I) find use in medicine as substitutes for pilocarpine.



(I)

Trimethylfurfurylammonium Iodide (I, X = I) is sold under the name of "furamon" in the Soviet Union and is used for the treatment of glaucoma (instead of the imported pilocarpine) [2], and also in veterinary practice [3]. Two methods for its preparation are described in the literature: directly from furfurylamine [4] or through dimethylfurfurylamine [1, 5].

We developed a method for the preparation of trimethylfurfurylammonium iodide in 60% yield, while according to the literature this product is obtained in a yield of only 25%. This method served as the basis for the production of "furamon" [6].

The starting material is furfural (2-furaldehyde), which by the method of reductive amination is converted into furfurylamine [7]. The furfurylamine was exhaustively methylated with methyl iodide in the presence of potassium carbonate. The purification, and also the properties of the trimethylfurfurylammonium iodide obtained here, are given in the experimental part.

Instead of methyl iodide we also used other, less expensive, methylating agents and synthesized the trimethylfurfurylammonium methyl sulfate and benzenesulfonate.

Trimethylfurfurylammonium Methyl Sulfate (I, $X = SO_4CH_3$) is formed when furfurylamine is reacted with dimethylsulfate in the presence of potassium carbonate. The reaction product is a nearly colorless crystalline substance, very hydroscopic, easily soluble in water and alcohol, and insoluble in diethyl ether and the esters. Its aqueous solutions show neutral, decolorized bromine water, and form a precipitate with barium chloride solution only after boiling with alkali. The elementary analysis data for sulfur and nitrogen support the empirical formula $C_9H_{17}O_5NS$. We were unable to determine the amount of carbon and hydrogen due to the extreme hygroscopicity of the salt. For the same reason the melting point determinations gave very ill-defined results (66-71°).

We also prepared trimethylfurfurylammonium methyl sulfate from trimethylfurfurylammonium iodide and dimethyl sulfate [8]. The salt obtained here was identical in all of its properties with the above-described salt. Due to its unusually great hygroscopicity this salt could not find use in medical practice.

Trimethylfurfurylammonium Benzenesulfonate (I, $X = SO_3C_6H_5$) is not described in the literature. We prepared it from furfurylamine and methyl benzenesulfonate. It is interesting to mention that irrespective of the molar ratios of reactants used, only the salt of the quaternary ammonium base, in greater or less yield, is always formed. This is observed irrespective of whether an alkaline, acid or neutral medium is used; neither the secondary nor the tertiary amine could be obtained by this method.

Trimethylfurfurylammonium benzenesulfonate is a colorless crystalline substance, easily soluble in water and alcohol, and insoluble in diethyl ether, benzene and the esters. Its aqueous solution reacts neutral and decolorizes bromine water. M. p. 134-135°. The elementary analysis data support the decomposition $C_{11}H_{19}O_4NS$. The salt, in contrast to the methyl sulfate, is not hygroscopic, and consequently it can find use in medical practice as a substitute for the more expensive quaternary iodide [9].

All three trimethylfurfurylammonium salts described here are close to each other in their curative action and toxicity.

EXPERIMENTAL

1. Synthesis of Trimethylfurfurylammonium Iodide. In a round-bottomed flask, fitted with dropping funnel, thermometer, reflux condenser and stirrer, was placed 9.7 g (0.1 mole) of furfurylamine, 100 ml of water and 15 g of chemically pure, finely pulverized potassium carbonate. With cooling in a water bath and mechanical stirring to the solution was added dropwise 50 g (0.35 mole) of methyl iodide, with maintenance of the temperature inside the mass at 15-20°; the reaction mass was carefully heated to 40-45° and maintained at this temperature for 3 hours, after which the excess methyl iodide was distilled off.

The reaction mass was steam-distilled until the escaping condensate showed neutral, decolorized with charcoal, evaporated to dryness, and dried to complete moisture removal in a vacuum-oven at 80° or in a vacuum-desiccator over calcium chloride or silica gel. The dried mixture of salts was extracted with 25-30 ml of anhydrous alcohol, and from the solution the trimethylfurfurylammonium iodide was precipitated with either 200 ml of anhydrous ethyl acetate or 150 ml of anhydrous butyl acetate.

The trimethylfurfurylammonium iodide was obtained as a white, finely crystalline, lustrous precipitate; it was separated, washed with anhydrous ethyl acetate, and dried in a vacuum-desiccator to constant weight. The yield was 16 g (60%), based on furfurylamine. M. p. 118-120°; from its iodine content, determined argentometrically, the substance calculated as 99.8% trimethylfurfurylammonium iodide.

2. Synthesis of Trimethylfurfurylammonium Methyl Sulfate. To a solution of furfurylamine (9.7 g, 0.1 mole) in 150 g of an aqueous 10% potassium carbonate solution at 15-20° was added in drops and with stirring 41 g (0.32 mole) of dimethyl sulfate. Then the liquid was heated to 40-45° and stirred at this temperature for 1 hour. The reaction mass was steam-distilled until the condensate showed neutral; the residue was decolorized with charcoal, evaporated, and dried to constant weight in a vacuum-desiccator over either silica gel or sulfuric acid. The dry residue was extracted with 55 ml of anhydrous alcohol, the alcohol vacuum-distilled, and the residue dried to constant weight in a vacuum-desiccator. The substance slowly solidified during the drying process, forming coarse, transparent, colorless or slightly yellowish crystals. Yield 17-17.5 g (68-70%). M. p. 66-71° (the substance was heated in a test tube, with the thermometer inside the mass). When heated over a free flame the substance darkens and decomposes with the evolution of trimethylamine.

0.3316 g sub.: 0.3064 g $BaSO_4$ [10]. 0.2413 g sub.: 0.2256 g $BaSO_4$. 0.4710 g sub.: 18.27 ml 0.1 N H_2SO_4. 0.5931 g sub.: 24.26 ml 0.1 N H_2SO_4. Found %: S 12.70, 12.84; N 5.43, 5.72. $C_9H_{17}O_5NS$. Calculated %: S 12.74; N 5.58.

We also synthesized the trimethylfurfurylammonium methyl sulfate from trimethylfurfurylammonium iodide and dimethyl sulfate by the method of gradually adding dimethyl sulfate (10 g) to trimethylfurfurylammonium iodide (20 g), with heating on the water bath. The substance obtained here was identical with the substance described above.

3. Synthesis of Trimethylfurfurylammonium Benzenesulfonate [6]. To a 10% aqueous solution of potassium carbonate (15 g) was added 11.7 g of furfurylamine, and with stirring and cooling (15-20°) was added in drops 62.5 g (3 mol. equivs.) of methyl benzenesulfonate. The liquid was stirred for 1 hour at 20° and then for another hour at 45°. The rest of the procedure was the same as described above for the preparation of the quaternary methyl sulfate. The dried mixture of salts was recrystallized from 120 ml of an alcohol-butyl acetate (1:4) mixture. Yield 18 g (50%). M. p. 134-135°.

0.1186 g sub.: 0.2437 g CO_2; 0.0706 g H_2O. 0.1154 g sub.: 0.2368 g CO_2; 0.0683 g H_2O. 0.1070 g sub.: 4.7 ml N_2 (26°, 738 mm). 0.1233 g sub.: 5.2 ml N_2 (23°, 742 mm). Found %: C 56.07, 56.00; H 6.66, 6.62; N 4.87, 4.7 4.74. $C_4H_{19}O_4NS$. Calculated %: C 56.56; H 6.40; N 4.71.

SUMMARY

1. It was shown that the reaction of furfurylamine with methyl iodide in aqueous potassium carbonate solution gives trimethylfurfurylammonium iodide in 60% yield.

2. The reaction product from furfurylamine and dimethyl sulfate, identified as trimethylfurfurylammonium methyl sulfate, was isolated and characterized.

3. The reaction product from furfurylamine and methyl benzenesulfonate, identified as trimethylfurfuryl-ammonium benzenesulfonate, was isolated and characterized.

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SYNTHESIS OF DIASTEREOISOMERIC α-PHENYL-β-(4-PIPERIDYL)-GLUTARIC ACIDS

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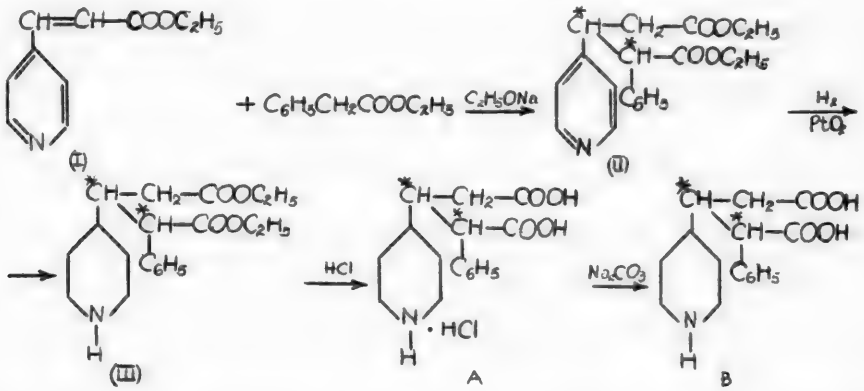
The present work was devoted to the synthesis and study of the properties of the diastereoisomeric α-phenyl-β-(4-piperidyl)-glutaric acids. Similar compounds are of interest as starting substances for the synthesis of 2,3-disubstituted quinuclidine derivatives by our earlier described method [1]. The diastereoisomeric α-phenyl-β-(4-piperidyl)-glutaric acids were obtained by the following scheme:



The ethyl ester of β-(4-pyridyl)acrylic acid (I) was condensed at 60° with the ethyl ester of phenylacetic acid in the presence of an equivalent amount of sodium ethylate; here the diethyl ester (II) of α-phenyl-β-(4-pyridyl)-glutaric acid was obtained in 90% yield. Compound (II) and all of the substances obtained from it, presented in the scheme, contain two asymmetric carbon atoms, which indicates the existence of two diastereoisomeric forms for these compounds.

The reduction of the hydrochloride of the diester (II) in alcoholic solution at room temperature in the presence of platinum catalyst (according to Adams) leads to the formation of the hydrochloride of the diethyl ester of α-phenyl-β-(4-piperidyl)-glutaric acid. Treatment of an aqueous solution of the obtained hydrochloride with 10% sodium carbonate solution gave colorless crystals, being the crystallohydrate of the diester (III). The latter when vacuum-distilled loses a mole of water, being converted into a colorless viscous liquid, which readily adds a mole of water in the air, again forming the crystallohydrate. The hydrochlorides of α-phenyl-β-(4-piperidyl)-glutaric acid (A) were obtained when the diethyl ester (III) of α-phenyl-β-(4-piperidyl)-glutaric acid was heated with concentrated hydrochloric acid. Two diastereoisomeric forms of the hydrochloride were isolated: 1) hydrochloride A_1: m. p. 230-231° (decompn.), and 2) hydrochloride A_2: m. p. 178°, differing, in addition to the melting point, also in its solubility in water. Hydrochloride A_2 is considerably more soluble in water than in hydrochloride A_1, and consequently it can be isolated only after the water from the removal of hydrochloride A_1 is completely evaporated.

The free diastereoisomeric acids (B) were obtained by treating the hydrochloride solutions of the corresponding acids in anhydrous alcohol with the calculated amount of alcoholic ammonia solution. From hydrochloride A_1 was isolated the free acid B_1 with m. p. 210-212°, and from hydrochloride A_2 the free acid B_2 with m. p. 272°. Acid B_1 is converted into the diastereoisomeric acid B_2 when heated in vacuo at 230-240°.

The reaction of bromine with the diethyl ester of α-phenyl-β-(4-piperidyl)-glutaric acid (III) was studied for the purpose of obtaining the diethyl ester of α-phenyl-α-bromo-β-(4-piperidyl)-glutaric acid. Compound (III) was treated with bromine at room temperature in chloroform solution. Instead of the expected bromo derivative the hydrobromide of the perbromide of the diethyl ester of α-phenyl-β-(4-piperidyl)-glutaric acid was obtained as

bright yellow crystals. The hydrobromide of the perbromide failed to decompose when boiled in chloroform solution for 5 hours, and also when heated without solvent to 145°. Treatment of the hydrobromide of the perbromide with 50% potash solution in the cold gave the free perbromide as a colorless oil with a strong halogen odor. The perbromide is easily converted into the original substance (III) when shaken with acetone or when heated with 50% potash solution.

We were also unable to obtain the diethyl ester of α-phenylα-bromo-β-(4-piperidyl)glutaric acid in the bromination of compound (III) with bromine in boiling acetic acid, or with dibromodioxane in chloroform or acetic acid solution at the boil. In these experiments the diester (III) remained unchanged.

EXPERIMENTAL

Diethyl α-Phenyl-β-(4-pyridyl)glutarate (II). To the sodium ethylate obtained from 2.6 g of metallic sodium and 40 ml of anhydrous alcohol was added 18.56 g of ethyl phenylacetate and 20 g of ethyl β-(4-pyridyl)-acrylate. The reaction mass was heated for 2 hours at 60°. Here the yellow homogeneous solution was converted into a dense, brown-colored solid mass. The resulting precipitate was treated with 300 ml of water containing 8 ml of glacial acetic acid, then filtered, washed with water, and dried. Yield 34.7 g (90%). Recrystallization from petroleum ether gave the diethyl ester of α-phenyl-β-(4-pyridyl)glutaric acid as a white crystalline powder, readily soluble in alcohol, acetone and chloroform, poorly soluble in ether and petroleum ether, and insoluble in water. M. p. 100°.

3.768 mg sub.: 9.711 mg CO_2; 2.290 mg H_2O. 4.130 mg sub.: 10.661 mg CO_2; 2.459 mg H_2O. 12.465 mg sub.: 0.431 ml N_2 (20.5°, 741 mm). Found %: C 70.33, 70.44; H 6.80, 6.65; N 3.92. $C_{20}H_{23}O_4N$. Calculated %: C 70.38; H 6.74; N 4.11.

α-Phenyl-β-(4-pyridyl)glutaric Acid. Two grams of the diethyl ester of α-phenyl-β-(4-pyridyl)glutaric acid was boiled for 4 hours with 20 ml of hydrochloric acid (1:1). The hydrochloric acid solution was evaporated to a fourth of its original volume and then cooled. The colorless hydrochloride crystals were separated, thoroughly pressed free of mother liquor, and again dissolved in 5 ml of water. The resulting aqueous solution was treated with a saturated sodium bicarbonate solution until it no longer showed acid to Congo. Here the α-phenyl-β-(4-pyridyl)glutaric acid deposited as fine needle crystals. M. p. 231-233° (decompn.). The acid is readily soluble in water and insoluble in organic solvents.

3.746 mg sub.: 9.223 mg CO_2; 1.819 mg H_2O. Found %: C 67.19; H 5.43. $C_{16}H_{15}O_4N$. Calculated %: C 67.37; H 5.26.

Diethyl α-Phenyl-β-(4-piperidyl)glutarate (III). To a solution of 28.3 g of diethyl α-phenyl-β-(4-pyridyl) glutarate in 235 ml of anhydrous alcohol was added 13.8 ml of a 22% alcoholic hydrogen chloride solution. The resulting alcohol solution of the hydrochloride of diethyl %-phenyl-β-(4-pyridyl)glutarate was hydrogenated at room temperature in the presence of 0.8 g of platinum oxide. The necessary amount of hydrogen was absorbed in 140 hours. Then the alcohol solution was filtered from the platinum black and evaporated in vacuo to dryness. The hydrochloride (III) was obtained in quantitative yield.

To obtain the free base the aqueous hydrochloride solution was treated with 10% soda solution until it showed alkaline to phenolphthalein. The resulting precipitate was filtered, washed with water, and dried. The crystallohydrate (III) was obtained as thin colorless needles (from acetone), readily soluble in alcohol and chloroform, and poorly soluble in ether, acetone and water. M. p. 79-80°.

2.875 mg sub.: 6.890 mg CO_2; 2.109 mg H_2O. 5.296 mg sub.: 1.53 ml 0.01 N H_2SO_4. Found %: C 65.40; H 8.20; N 4.04. $C_{20}H_{29}O_4N \cdot H_2O$. Calculated %: C 65.72; H 8.50; N 3.98.

The obtained crystallohydrate (III) was vacuum-distilled without decomposition, losing here a mole of water of crystallization. B. p. 172° at 0.1 mm. Colorless, exceedingly viscous liquid, which slowly crystallized in the air, reverting back to the above described crystallohydrate with m. p. 80°.

3.740 mg sub.: 9.448 mg CO_2; 2.849 mg H_2O. Found %: C 68.94; H 8.52. $C_{20}H_{29}O_4N$. Calculated %: C 69.14; H 8.36.

Diethyl α-Phenyl-β-(4-N-acetylpiperidyl)glutarate. The hydrochloride (III) (2.1 g) was treated with 10 ml of 50% aqueous potash solution and then extracted with chloroform. The chloroform solution was dried over potash, the chloroform distilled in vacuo, and the residue heated with 20 ml of acetic anhydride for 1 hour. The acetic anhydride was vacuum-distilled, the residue dissolved in ether, the ether solution washed with water, then with 10%

soda solution, and dried over potash. After removing the ether the substance was vacuum-distilled. B. p. 215-218° (0.3 mm). Exceedingly viscous colorless liquid that crystallized on standing. Yield 1.5 g (70.4%). M. p. 85°. The substance is readily soluble in ether, chloroform and alcohol, and difficultly soluble in water.

3.659 mg sub.: 9.150 mg CO_2; 2.619 mg H_2O. 3.311 mg sub.: 8.331 mg CO_2; 2.456 mg H_2O. Found %: C 68.24, 68.25; H 8.00, 8.25. $C_{22}H_{31}O_5N$. Calculated %: C 67.86; H 8.17.

α-Phenyl-β-(4-piperidyl)glutaric Acid Hydrochlorides (A_1 and A_2). A mixture of 0.9 g of diethyl α-phenyl-β-(4-piperidyl)glutarate and 9 ml of concentrated hydrochloric acid was boiled for 15 hours. The hydrochloric acid solution was decolorized with charcoal and evaporated on the water bath to incipient crystallization. The colorless crystals obtained on cooling were separated and washed with acetone. Yield of A_1 0.3 g; m. p. 230-231° (decompn).

3.835 mg sub.: 8.243 mg CO_2; 2.453 mg H_2O. 9.860 mg sub.: 0.385 ml N_2 (20°, 727 mm); 5.497 mg sub.: 0.85 ml 0.01 N $AgNO_3$. Found %: C 58.74; H 7.16; N 4.35; Cl 10.97. $C_{16}H_{21}O_4N \cdot HCl$. Calculated %: C 58.98; H 6.74; N 4.28; Cl 10.84.

The filtrate, remaining after the removal of hydrochloride A_1, was evaporated in vacuo to dryness, and the oily residue was rubbed with acetone. The fine colorless crystals obtained here were separated, washed with acetone, and dried. Yield 0.4 g. The obtained crystals melted in the range 170-212°. They were dissolved in 7 ml of anhydrous alcohol and the alcohol solution was diluted with 16 ml of anhydrous ether. An oil that crystallized on standing was obtained. Yield of A_2 0.2 g, m. p. 178° (decompn).

3.991 mg sub.: 1.735 mg AgCl. 17.014 mg sub.: 2.55 ml 0.02 N $AgNO_3$. Found %: Cl 10.75, 10.63. $C_{16}H_{21}O_4N \cdot HCl$. Calculated %: Cl 10.84.

After the removal of A_2 the filtrate was diluted with another 40 ml of anhydrous ether to give 0.17 g of substance with m. p. 208-212°, being, apparently, a mixture of hydrochlorides A_1 and A_2.

Diastereoisomeric α-Phenyl-β-(4-piperidyl)glutaric Acids (B_1 and B_2). Hydrochloride A_1 (0.2 g) was dissolved in 12 ml of anhydrous alcohol with heating. The alcohol solution was filtered from some turbidity and then treated with 0.23 ml of 4.48% alcoholic ammonia solution. Acid B_1 was obtained as a white crystalline powder. M. p. 210-212° (decompn).

A_2 (0.2 g) was treated with the same manner. Acid B_2 was obtained. M. p. 272° (decompn).

4.116 mg sub.: 9.954 mg CO_2; 2.671 mg H_2O. 8.560 mg sub. 0.374 ml N_2 (23°, 736 mm). Found %: C 66.00; H 7.26; N 4.88. $C_{16}H_{21}O_4N$. Calculated %: C 65.98; H 7.22; N 4.82.

Conversion of Acid B_1 Into Acid B_2. Hydrochloride A_1 (m. p. 230-231°) (0.2 g) was heated in vacuo (20 mm) at 230-235° for 15 minutes. The glassy mass obtained here was dissolved in 2 ml of anhydrous alcohol, the alcohol solution decolorized with charcoal, and then diluted with 10 ml of anhydrous ether. The resulting precipitate was separated, dissolved in 0.8 ml of saturated bicarbonate solution, and the thus obtained solution treated with acetic acid. There was obtained 0.07 g of acid B_2 as fine colorless crystals, readily soluble in water. M. p. 272° (decompn.).

Diethyl α-Phenyl-β-(4-piperidyl)glutarate Perbromide Hydrobromide. To a solution of 17.5 g of the hydrochloride of the diethyl ester of α-phenyl-β-(4-piperidyl)glutaric acid in 54 ml of dry chloroform was added at 20° with stirring over 8 hours a solution of 7.32 g of bromine in 55 ml of chloroform. Toward the end of bromine addition the solution became dark red in color, which color failed to vanish in the next 16 hours. The reaction mass was evaporated to a volume of 40 ml and then diluted with 100 ml of dry ether. The hydrobromide of the perbromide of (III) precipitated as bright yellow crystals, m. p. 145-147° (decompn). The hydrobromide of the perbromide of (III) is readily soluble in chloroform, alcohol and acetone, and insoluble in ether and water.

3.130 mg sub.: 4.698 mg CO_2; 1.370 mg H_2O. 3.317 mg sub.: 4.964 mg CO_2; 1.550 mg H_2O. 9.690 mg sub.: 0.206 ml N_2 (27°, 729 mm). 3.274 mg sub.: 3.141 mg AgBr. Found %: C 40.96; 40.84; H 4.90, 5.23; N 2.32; Br 4083. $C_{20}H_{30}O_4NBr_3$. Calculated %: C 40.82; H 5.1; N 2.38; Br 40.82.

SUMMARY

The synthesis of the diastereoisomeric α-phenyl-β-(4-piperidyl)glutaric acids was realized, and also their mutual interconversion.

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* T. p. = C. B. Translation pagination.

THE SYNTHESIS OF SOME 4-BIPHENYLAMINE DERIVATIVES

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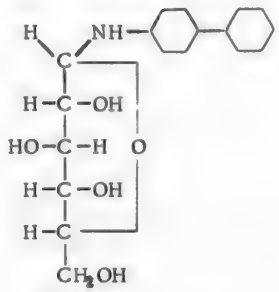
Quite a few papers have been published in recent years on the synthesis of organic compounds possessing activity against tubercle bacilli. As is known, some of the substances proved to be extremely effective and found use in the chemotherapy of tuberculosis, in which number 4-aminosalicyclic acid is included [1]. Also, many derivatives of 4-aminosalicylic acid were prepared and tested [2-4].

There is an indication that the activity of 4-biphenylamine is nearly 20 times greater than that of 4-aminosalicylic acid [2]. However, 4-biphenoylamine is hardly suitable for use in view of its toxicity and ease of oxidation.

It was of interest to protect the amino group of 4-biphenylamine for the purpose of obtaining a more stable and less toxic compound, and also to realize the synthesis of 4-biphenylamine derivatives by its condensation with 4-aminosalicylic acid. Glucose was selected to protect the amino group in 4-biphenylmine.

Depending on the synthesis conditions, the condensation of aromatic amines with glucose proceeds either between the amino group and the hydroxyl at the glucosidic carbon with the formation of glucosylarylamines, or in the case of using more drastic synthesis conditions between the amino group and the oxygen of the aldehyde group with the formation of azomethines. The latter are readily decomposed by alkalies, while the glucosylarylamines are unstable toward acids [5, 6].

The glucoside (I) of 4-biphenylamine is not reported in the literature. It was obtained by the reaction of anhydrous glucose with 4-biphenylamine in 96% alcohol.

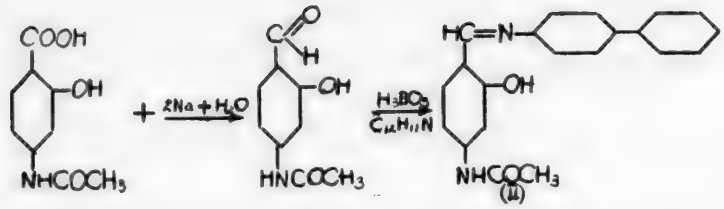


(I)

The glucoside of 4-biphenylamine reduces Fehling solution and is easily decomposed by 5% hydrochloric acid solution, which is evidence that the obtained glucoside is a glucosylarylamine, and not the azomethine.

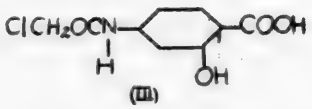
The best results as regards both the quality and yield of the glucoside were obtained when the synthesis was run with freshly distilled 4-biphenylamine in anhydrous alcohol medium; the use of 96% alcohol is also permissible. Further reduction in alcohol concentration leads to oxidation of the 4-biphenylamine and hydrolysis of the already formed glucoside.

As is known, amines react readily with the acid chlorides of carboxylic acids. It seemed expedient to effect condensation between 4-niphenylamine and 4-aminosalicylic acid through the acid chloride of the latter. To protect its amino group the 4-aminosalicylic acid was acetylated. However, we were unable to obtain the acid chloride of 4-acetamidosalicylic acid; so we chose a different synthesis path, by analogy with the already described reaction of p-toluidine with salicylaldehyde, obtained by the reduction of salicylic acid, with the formation of N-salicylidene-p-toluidine [7]. To avoid secondary processes the synthesis was not run with 4-aminosalicylic acid, but instead was run with its acetyl derivative:

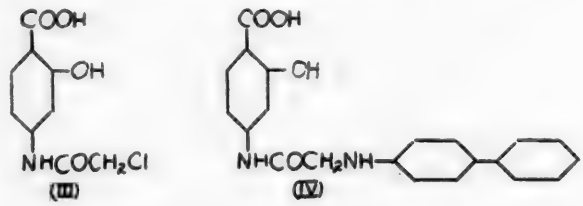


Repetition of the conditions for the synthesis of N-salicylidene-p-toluidine failed to give a positive result. Raising the temperature from 20 to 50-55°, increasing the time of adding the metallic sodium, and introducing additional holding at 50°, all had a favorable influence on the process. 4-(4-Acetamidosalicylidene)aminobiphenyl (II) was obtained for the first time.

To determine the influence of the carboxyl group in compounds of this type on the antitubercular activity, it appeared of interest to condense 4-niphenylamine with 4-aminosalicylic acid to at the amino group. Attempts to effect direct condensation of the indicated compounds failed to give positive results; consequently, the previously unknown 4-(chloroacetamido)salicylic acid (III) was first prepared.



The condensation of 4-(chloroacetamido)salicylic acid with 4-biphenylamine was run in 96% ethyl alcohol and led to the previously unknown 4-[2-(4-biphenylamino)acetamido]salicylic acid (IV):



The same as for the synthesis of the glucoside of 4-biphenylamine, both the degree of purity of the 4-biphenylamine and the alcohol concentration show decisive influence on the condensation reaction.

The compounds synthesized by us showed in vitro tuberculostatic activity; however, the data were not supported in the experiments with mice.

EXPERIMENTAL

4-Biphenylamine Glucoside. A mixture of 33.8 g (0.2 mole) of 4-biphenylamine, freshly distilled at 8-10 mm and having freezing point 52.5-53°, and 4 g of anhydrous glucose was dissolved at 50-60° in 200 ml of 96% alcohol. To this solution was added 4 g of activated wood charcoal, and after heating for 15 minutes under reflux the charcoal was filtered. To the filtrate was added 32 g of glucose (a total of 36 g or 0.2 mole), and with periodic stirring the solution was heated on the boiling water bath for 6 hours. After a second treatment with charcoal the clear colorless solution was let stand for two days to crystallize. The 4-biphenylamine glucoside crystallized in the form of needles, at times as clumps; it was filtered, washed with alcohol and ether, and dried in a desiccator over calcium chloride. Yield 52-53 g (70-80%). M. p. 111-112° (decompn.). Readily soluble in alcohol and benzene, and insoluble in ether.

If the 4-biphenylamine glucoside is obtained with a lower melting point, then it is treated several times with ether (to remove slight traces of unreacted 4-biphenylamine) and recrystallized from alcohol.

3.270 mg sub.: 0.123 ml N_2 (24°, 750 mm). 4.360 mg sub.: 0.163 ml N_2 (23°, 750 mm). 4.718 mg sub.: 11.284 mg CO_2; 2.665 mg H_2O. 5.907 mg sub.: 14.158 mg CO_2; 3.315 mg H_2O. Found %: C 65.26, 65.41; H 6.32, 6.28. N 4.27, 4.26. $C_{18}H_{21}O_5N$. Calculated %: C 65.26; H 6.40; N 4.24.

4-(4-Acetamidosalicylidene)aminobiphenyl. In a three-necked flask, fitted with stirrer, was placed 900 ml of 0.6% sodium carbonate solution and 17.85 g (0.092 mole) of 4-acetamidosalicylic acid. To this solution of sodium 4-acetamidosalicylate was added at 80° 24.0 g (0.142 mole) of freshly distilled 4-biphenylamine; then with good (and careful) stirring at 50-55° was added 225 g of sodium chloride and in the course of two hours 370 g of 2% sodium amalgam and 120 g of boric acid, making sure that the reaction always remained acid to litmus. After all of the sodium amalgam had been added, the mass was stirred for another 2 hours at 50-55°. The resulting azomethine was separated, washed with cold water, and dried at 40-45°. For purification the azomethine was treated 3-4 times with ether, and then recrystallized from alcohol. Yield 14.0-14.5 g (46.5-47.0%), based on 4-acetamidosalicylic acid. M. p. 233-234°.

4.215 mg sub.: 0.323 ml N_2 (25°, 735 mm). 5.045 mg sub.: 0.388 ml N_2 (25°, 747 mm). Found %: N 8.64, 8.66. $C_{21}H_{18}O_2N_2$. Calculated %: N 8.48.

Spectral analysis showed the absence of mercury in the compound.

4-[2-(4-biphenylamino)acetamido]salicylic acid. In a round-bottomed flask, fitted with reflux condenser, was placed 300 ml of alcohol, 17.3 g (0.075 mole) of 4-(2-chloroacetamido)-salicylic acid with m. p. 235-236°, and 25.5 g (0.15 mole) of freshly distilled 4-biphenylamine. After heating for 10-15 minutes the obtained solution was treated with charcoal, and the filtrate was boiled for 7 hours. The resulting 4-[2-(4-biphenylamino)acetamido] salicylic acid was filtered, washed with hot alcohol, and dried at 60-70°.

4-[2-(4-Biphenylamino)acetamido]salicylic acid is insoluble in benzene, toluene, xylene, chloroform, carbon tetrachloride, alcohol and ether. We were unable to recrystallize it. It was purified from impurities by successive boiling under stirring with benzene, alcohol, and ether. Yield 12 g (44.5%). M. p. 231;5-232.0°.

3.410 mg sub.: 0.233 ml N_2 (22°, 745 mm). 4.725 mg sub.: 0.320 ml N_2 (23°, 719 mm). 0.5373 g sub.: 14.82 ml 0.1 N NaOH. 0.5120 g subn: 14.08 ml 0.1 N NaOH. Found %: N 7.75, 7.67. M 362.6, 361.6. $C_{21}H_{18}O_4N_2$. Calculated %: N 7.74. M 362.6.

4-Acetamidosalicylic Acid. A solution of 87.5 g (0.5 mole) of sodium 4-aminosalicylate in 450 ml of water was prepared. To the filtered solution was added with vigorous stirring at 30° 60.6 g (0.6 mole) of acetic anhydride and the mixture stirred for another 5 hours. Yield 73.7 g (75.6%). After recrystallization from 35% alcohol (1:20), m. p. 225-226°.

5.940 mg sub.: 0.352 ml N_2 (22°, 740 mm). 5.730 mg sub.: 0.336 ml N_2 (22°, 740 mm). Found %: N 7.26, 7.20. $C_9H_9O_4N$. Calculated %: N 7.18.

4-(2-Chloroacetamido)salicylic Acid. To a solution of 25 g (0.14 mole) of sodium 4-aminosalicylate in 280 ml of water was added 32 g of sodium bicarbonate at 35-40°. After the latter had dissolved the mass was cooled to 20° and 32 g (0.283 mole) of chloroacetyl chloride was added from a dropping funnel over a period of 10-15 minutes. The mass was stirred for 1 hour, and the resulting 4-(2-chloroacetamido)salicylic acid was filtered, washed with water, and dried at 50-60°. Yield 22-23 g (69.5-72.0%), m. p. 235-236°.

4.665 mg sub.: 0.252 ml N_2 (21°, 750 mm). $C_9H_8O_4ClN$. 0.1860 g sub.: 8.2 ml 0.1 N $AgNO_3$. 0.2100 g sub.: 9.1 ml 0.1 N $AgNO_3$. 0.2186 mg sub.: 9.5 ml 0.1 N NaOH. 0.1790 mg sub.: 7.9 ml 0.1 N NaOH. Found %: N 6.19; Cl 15.2, 15.6. M 229.5, 226.6. $C_9H_8O_4ClN$. Calculated %: N 6.10; Cl 15.5. M 229.5.

SUMMARY

1. Some previously unknown derivatives of 4-biphenylamine were obtained and characterized.

2. A method was developed for the preparation of the glucoside of 4-biphenylamine.

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REACTION OF DIBROMOALLYL ALCOHOL WITH DISODIOMALONIC ESTER

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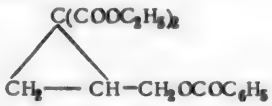
The Perkin reaction of dihalo derivatives of open chain hydrocarbons, in which the halogens are found on different carbon atoms, with disodiomalonic ester leads to the formation of cyclic acid esters. In developing these syntheses it appeared of interest to introduce into the reaction such substances as had a group with an active hydrogen atom in the α-position to one of the halogen-containing carbons. Dibromoallyl alcohol was taken in the present work and its behavior toward disodiomalonic ester was studied.

Experiment revealed that in the reaction of dibromoallyl alcohol with disodiomalonic ester 62% of the dibromoallyl alcohol is recovered unchanged, while the remainder is consumed in the formation of a brown resin.

The benzoate of dibromoallyl alcohol reacted smoothly with disodiomalonic ester to give the crystalline ester of 1-hydroxymethyl-2,2-cyclopropanedicarboxylic acid:



Since the Conrad and Perkin syntheses with malonic ester are usually run in anhydrous alcohol, it then follows that the presence of substances with a hydroxyl group in the reaction medium during the time of running such a synthesis will fail to show a negative influence on the reaction course. Consequently, the peculiar behavior shown by dibromoallyl alcohol in the given synthesis should be explained as being exclusively due to the hindering action of the hydroxyl group in its α-position to one of the halogen-containing carbon atoms on the properties of the dibromide.

EXPERIMENTAL

Bromination of Allyl Alcohol. To 58 g of allyl alcohol with ice cooling was added in drops 160 g of bromide. The reaction product was distilled. After removing several grams of unreacted allyl alcohol the dibromoallyl alcohol distilled at 205.5-206°. According to Lespieau [1]: b. p. 205-208°. Since Lespieau fails to show other constants, then d_4^{20} 1.8960, n_D^{20} 1.5360 were determined.

Preparation of Disodiamalonic Ester. To 17 g of sodium, cut into small pieces and found under a layer of dry benzene, was added 55 g of malonic ester. Instantly the evolution of hydrogen bubbles began. The reaction mixture was let stand a day. The resulting salve like mass still contained some small pieces of sodium and was heated on the water bath until a yellow solution was obtained.

Preparation of the Benzoate of Dibromoallyl Alcohol and Its Reaction with Disodiomalonic Ester. A survey of the literature revealed that this ester was still unknown. The ester was prepared by the Schotten-Baumann reaction. To 25 g of dibromoallyl alcohol was added 16 g of benzoyl chloride and to the emulsion of these two substances was added 10 ml of 50% sodium hydroxide solution. The mixture was vigorously shaken for about 1 hour, and then allowed to stand overnight. A precipitate in the form of tiny needles was obtained, which were separated from the liquid, washed with water, and air-dried. Yield 4 g (10.8%). The crystals are poorly soluble in cold benzene and readily soluble in hot benzene. After two recrystallizations from benzene the crystals had m. p. 86-88°.

To a benzene solution of disodiomalonic ester, prepared from 8 g of malonic ester and 2.5 g of metallic sodium, was added 15 g of the benzoate of dibromoallyl alcohol. The mixture was heated on the water bath for 5 hours. After cooling the solution the liquid was filtered from the precipitate and poured into a crystallizing dish. Removal of the benzene by evaporation left needlelike crystals. Two recrystallizations from benzene gave 7.5 g of crystals as coarse needles with m. p. 115-117°.

0.0206 g sub.: 0.0477 g CO_2; 0.0111 g H_2O. 0.1310 g sub.: 21.15 g benzene: Δt 0.174°. Found %: C 63.22; H 6.00. M 321.6. $C_{17}H_{20}O_6$. Calculated %: C 63.76; H 6.26. M 321.6.

SUMMARY

The reaction of the benzoate of dibromoallyl alcohol with disodiomalonic ester gave the ester of 1-hydroxymethyl-2,2-cyclopropanedicarboxylic acid.

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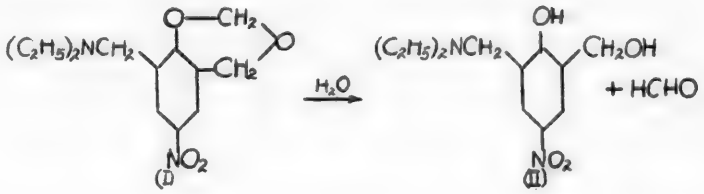
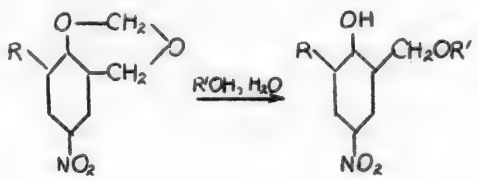
THE SYNTHESIS OF 5-NITROSALIGENIN AND ITS ETHERS

V. I. Stavrovskaya

In elucidating the structure of 3-diethylaminomethyl-5-nitrosaligenin methylene ether (I), described by Einhorn [1] as "2-hydroxy-5-nitrobenzyldiethylamine", it was shown by us that the heating of this substance with dilute sulfuric acid leads to the evolution of formaldehyde and the formation of a new compound [2]. Further study established that this new compound is 3-diethylaminomethyl-5-nitrosaligenin (II), the formation of which proceeds in accord with the following scheme:



The use of this method for the synthesis of 5-nitrosaligenin from 5-nitrosaligenin methylene ether led, under prolonged heating, to the formation of a pliant mass instead of the desired 5-nitrosaligenin. With short heating the original product was recovered unchanged. We were of the opinion that the negative results of the last reaction was associated with the insolubility of the 5-nitrosaligenin methylene ether in dilute sulfuric acid. Actually, the addition of alcohol as a solvent led to ring opening, but together with this, also to etherification of the formed 5-nitrosaligenin. With this method the previously unknown methyl and ethyl ethers of 5-nitrosaligenin and the methyl ether of 3-diethylaminomethyl-5-nitrosaligenin were synthesized.



where R = H, $(C_2H_5)_2NCH_2$; R' = CH_3, C_2H_5.

Prolonged boiling of the 5-nitrosaligenin methylene ether with 10% sodium hydroxide solution also caused ring rupture, and here we isolated 5-nitrosaligenin as the reaction product. However, in this case the reaction proceeds with poor yield.

The above described reactions can serve as a method for the synthesis of substituted saligenin derivatives and their ethers.

EXPERIMENT

3-Diethylaminomethyl-5-nitrosaligenin. 3-Diethylaminomethyl-5-nitrosaligenin methylene ether (2 g) was boiled with dilute sulfuric acid (5 ml, 1:1 by volume) for an hour; here the strong odor of formaldehyde was noted. The clear liquid after cooling was diluted with water (20 ml), made alkaline with 10% sodium hydroxide solution, and filtered from undissolved particles. The filtrate was acidified with hydrochloric acid until it showed acid to Congo and then it was saturated with potash until a yellow solid separated. The precipitate was filtered (1.2 g), recrystallized from water, and then from benzene. Fine bright yellow needles; m. p. 81-82°.

3-Diethylaminomethyl-5-nitrosaligenin is readily soluble in alcohol, and soluble in benzene, water, and in dilute acids and alkalies. With ferric chloride it gives a cherry-red color.

3.813 mg sub.: 0.382 ml N_2 (20°, 739 mm). 2.940 mg sub.: 0.294 ml N_2 (21°, 739 mm). Found %: N 11.35, 11.29. $C_{12}H_{18}O_4N_2$. Calculated %: N 11.02.

The hydrochloride is white. It can be recrystallized from either alcohol or 10% hydrochloric acid. M. p. 166-167° (decompn).

4.208 mg sub.: 0.372 ml N_2 (21°, 747 mm). 4.245 mg sub.: 0.363 ml N_2 (22°, 750 mm). Found %: N 10.09, 9.76. $C_{12}H_{19}O_4N_2Cl$. Calculated %: N 9.64.

5-Nitrosaligenin Ethyl Ether. In a small flask, fitted with reflux condenser, was placed 5-nitrosaligenin methylene ether (3 g), ethyl alcohol (15 ml) and concentrated sulfuric acid (2.5 ml). The solution was boiled for 6 hours, after which water was added (50 ml), and the yellow liquid separating on the bottom of the flask was extracted with ether. The ether solution was washed with distilled water and dried over sodium sulfate. Distilling off the ether gave a residue of 1.9 g of yellow mobile liquid, which was dissolved in 5% sodium hydroxide solution, filtered from a small amount of flock, acidified with 10% hydrochloric acid, and the obtained oil extracted with ether. The ether solution was washed with distilled water and dried over sodium sulfate. Removal of the ether by distillation left 1.4 g of viscous yellow liquid, which solidified on standing in a vacuum-desiccator. The substance was recrystallized from petroleum ether to give white leaflets with m. p. 85°. The ethyl ether of 5-nitrosaligenin is readily soluble in ether, benzene, acetone, alcohol and dilute alkali, soluble in petroleum ether, and insoluble in water and dilute acids. A cherry-brown color is obtained with ferric chloride.

4.412 mg sub.: 0.284 ml N_2 (28°, 734 mm). 4.746 mg sub.: 0.304 ml N_2 (28°, 739 mm). Found %: N 7.04, 7.16. $C_9H_{11}O_4N$. Calculated %: N 7.11.

5-Nitrosaligenin Methyl Ether. 5-Nitrosaligenin methylene ether (3 g), methyl alcohol (15 ml) and concentrated sulfuric acid were heated in a small flask under reflux, with boiling of the liquid inside the flask. The flask contents failed to go into solution after heating for 3 hours., consequently there were added alcohol (10 ml), sulfuric acid (2 ml) and water (0.5 ml). The heating was continued for another 12 hours, after which the reaction liquid was a clear yellow solution to which after cooling, water was added (50 ml). Further treatment was the same as for the preparation of the ethyl ether. The yield of yellowish liquid was 2.7 g, which quickly solidified. The substance crystallizes as plates from either petroleum ether or heptane, and as white prisms from water. M. p. 109°. The methyl ether of 5-nitrosaligenin is very soluble in alcohol, acetone, benzene and in dilute alkalies, soluble in heptane and water, poorly soluble in petroleum ether, and insoluble in dilute acids. With ferric chloride it gives a cherry-red color.

5.984 mg sub.: 0.421 ml N_2 (25°, 733 mm). 6.135 mg sub.: 0.431 ml N_2 (22°, 728 mm). Found %: N 7.77, 7.79. $C_8H_9O_4N$. Calculated %: N 7.65.

3-Diethylaminomethyl-5-nitrosaligenin Methyl Ether. 3-Diethylaminomethyl-5-nitrosaligenin- methylene ether (2 g), methyl alcohol (10 ml), concentrated sulfuric acid (6 ml) and water (0.5 ml) were boiled for 8 hours. To the flask after cooling was added water (20 ml), and then 10% sodium hydroxide solution to alkaline reaction. The solution was filtered, acidified with 10% hydrochloric acid, and saturated with potash. The resulting yellow oil was extracted with ether. The ether solution was dried over sodium sulfate. Removal of the ether by distillation left 1.2 g of thick yellow liquid, which was dissolved with heating in a very small amount of water. Yellow needles separated on cooling. M. p. 80.5-82°.

The methyl ether of 3-diethylaminomethyl-5-nitrosaligenin is readily soluble in ether, water, benzene, and in dilute alkalies and acids, and poorly soluble in petroleum ether. With ferric chloride it gives a cherry-red color.

5.962 mg sub.: 0.558 ml N_2 (23°, 745 mm). 5.801 mg sub.: 0.549 ml N_2 (23°, 746 mm). Found %: N 10.58, 10.71. $C_{12}H_{18}O_4N_2$. Calculated %: N 10.45.

5-Nitrosaligenin. 5-Nitrosaligenin methylene ether (1.5 g) was boiled in 10% sodium hydroxide solution (20 ml) for 5 hours. The yellow solution after cooling was filtered from the solid (1.2 g), acidified with 10% hydrochloric acid until acid to Congo, and extracted with ether. The ether solution was dried over sodium sulfate. Removal of the ether by distillation left 0.3 g of mobile yellow liquid, which congealed on rubbing and became solid when petroleum ether was added. The substance was filtered (0.2 g) and recrystallized from benzene. Yellow needles, m. p. 125° (the literature gives m. p. 126° [1]).

5-Nitrosaligenin is readily soluble in alcohol, ether and acetone, soluble in benzene and water, poorly soluble in petroleum ether, and soluble in dilute acids and alkalies. With ferric chloride it gives a red color.

Found %: N 8.63, 8.49. $C_7H_7O_4N$. Calculated %: N 8.28.

The solid product, failing to dissolve when boiled with alkali, burns, but does not melt. Its structure was not established.

SUMMARY

1. A method for the synthesis of substituted derivatives of saligenin and its ether was described.

2. The methyl and ethyl ethers of 5-nitrosaligenin, 3-diethylaminomethyl-5-nitrosaligenin, and its methyl ether, were synthesized and characterized.

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CHITIN

II. GLYCEROL ETHERS OF CHITIN

S. N. Danilov and E. A. Plisko

The synthesis of esters and ethers proceeds with considerably more difficulty for chitin than it does for cellulose, which it is impossible not to associate with the low degree of swelling shown by chitin in acids and especially in alkalies [1].

Information on the esters of chitin was to a large degree summarized in the studies of P. P. Shorygin and his coworkers [2-4]. They indicate that the acetylation [3] and nitration [2] conditions, used with success in the case of cellulose, proved to be unsuitable for chitin, so that it became necessary to select more suitable acetylating and nitrating mixtures, running the reaction for many hours.

The indicated studies also contain a description [4] of the ethers (methyl) and chitin. The methylation of chitin with dimethyl sulfate in the presence of sodium hydroxide proceeds slowly and incompletely. After 45-fold methylation a chitin methyl ether with 9.34% of methoxyl groups (degree of substitution about 0.7 hydroxyl) was obtained. The reason for the difficult methylation of chitin should be sought in its weak swelling in alkali.

By using the technique of preliminary treatment of the chitin with hydrochloric acid, which causes marked swelling of the chitin, or with concentrated caustic solution, the indicated authors obtained chitin as a mass, readily crushed into a powder. In this case after 15 methylations a chitin methyl ether containing 16.07% methoxyl groups (substitution about 1.1 hydroxyls) was obtained.

The obtained chitin monomethyl ether was soluble in formic acid, and showed strong swelling in glacial acetic acid.

Later, it was briefly mentioned in other studies [5] that the reaction of alkali chitin with dimethyl sulfate yields methylchitin, soluble in cold and insoluble in hot water, similar to methylcellulose and hydroxybutylcellulose [6]; here it was indicated that chitin forms ethers (hydroxyethyl) with ethylene chlorohydrin and ethylene oxide, but neither the synthesis conditions nor the properties of the ethers themselves were given.

The purpose of our studies was to specifically obtain the unknown water-soluble (hydrophilic) ethers of chitin – the hydroxyethyl and glycerol ethers of different degrees of substitution, which fact would be of interest for rendering chitin soluble in aqueous media [7].

The glycerol ethers of chitin are described in our above mentioned communication. Such ethers for cellulose were synthesized by Shorygin [8] and Danilov [9], together with their coworkers, as linear and three-dimensional molecules. The reaction of alkali chitin with glycerol monochlorohydrin and glycidic alcohol was used to synthesize the glycerol ethers of chitin.

The synthesis proceeded well, provided well pulverized chitin was used, which had first been precipitated from solution in 78.4% phosphoric acid, or if the chitin in the caustic was cooled at −40 to −70°, or if the impregnation with the caustic was run for several hours under reduced pressure, with an etherification time of 30-40 hours, and a temperature of about 60°. The higher degrees of substitution (around 1-1.6 hydroxyl groups) were predominantly obtained under repeated etherification. In not a single case were the ethers soluble in water, in contrast to the corresponding cellulose ethers; some of the specimens either partially or completely dissolved in 4 and 8% sodium hydroxide solution, and in 3-50% acetic acid. All of the glycerol ether specimens were soluble in dilute mineral acids, which, apparently, was facilitated by the appearance of deacetylated amino groups.

The properties of the ethers, obtained through the monochlorohydrin, differ from the properties of the ethers obtained through the use of glycidic alcohol, and specifically in their lower degree of swelling or complete absence of swelling in dilute sodium hydroxide, in organic acids, and in water. Evidently, here there was a certain "stitching together" of the molecules due to the presence of trace impurities of glycerol dichlorohydrin in the glycerol monochlorohydrin, which impurities we were unable to remove under our distillation conditions.

A characteristic of chitin etherification is the strongly defined heterogeneity of the reaction products, which is also characteristic of the cellulose ethers, but to a lesser degree. The ethers based on the glycidic alcohol are especially heterogeneous, in addition to which the glycidic alcohol suffers considerably self-condensation under the synthesis conditions.

Determination of the composition of the chitin glycerol ethers is complicated by the fact that in their synthesis a partial deacetylation of the amino groups is observed, as can be seen when the percentage amounts of nitrogen, acetyl and glycerol groups in the obtained ethers are compared. The general composition of the obtained glycerol ethers of chitin is expressed by the formula:

$$[C_6H_7O_2(NHCOCH_3)_y(NH_2)_{1-y}(OH)_{2-x}(OCH_2CHOHCH_2OH)_x]_n$$

or $$[C_6H_9O_6(NHCOCH_3)_y(NH_2)_{1-y}(>CHCHOHCH_2OH)_x]_n$$

where the highest value of x was 1.6, while y varied in the limits 0.3-0.6 of the original value. For some of the glycerol ethers the characteristic viscosities in 4 and 8% caustic solutions were determined, in numerical value proving to be close to those obtained for solutions of chitin itself, but in phosphoric acid.

EXPERIMENTAL

1. Chitin Glycerol Ethers Based on Glycerol Monochlorohydrin

The monochlorohydrin needed for the syntheses was prepared from glycerol in the usual manner, was repeatedly distilled to free it of the dichlorohydrin, and had the following constants:

B. p. 110° (8 mm), n_D^{20} 1.4789, d_4^{20} 1.3214, MR_D 23.89; calc. 23.97.

In some of the synthesis experiments the chitin specimens used had been obtained by precipitation from solutions in 78.4% phosphoric acid, but for Specimen 1 a low degree of etherification (6.14% of glycerol groups) was obtained under the conditions described below.

A favorable influence for reaction to proceed is shown by the gringing of the chitin and especially by the repeated freezing and thawing of the caustic used in the swelling of the chitin.

We will describe one of the experiments on the synthesis of the ether in which glycerol monochlorohydrin was used as the etherification agent.

Six grams of dry chitin was covered with 90 ml of 30% sodium hydroxide solution in a small flask (100 ml), which was then tightly closed and placed in a Dewar vessel containing solid carbon dioxide, where alternate freezing (for 30 minutes) and thawing (for 60 minutes) was repeated 5 times in a time interval of 7.5 hours. The caustic was squeezed out from the strongly swollen chitin to a 3-fold weight. The resulting alkali chitin cake was ground in a porcelain mortar and then placed in a reaction flask, fitted with stirrer, where the monochlorohydrin (15 g) in acetone (100 ml) was introduced in a 4:1 ratio of monochlorohydrin to chitin. The flask was heated on the water bath (60°) for 40 hours (with interruptions). The control used to determine the end of synthesis was a negative Beilstein test for chlorine in the organic substance.

The preparation, filtered from the acetone, was introduced into water, where the alkali was neutralized with acetic acid, after which the product was washed and dried. Yield 5.8 g. The substance (Specimen 1) fails to swell in water and in 4% sodium hydroxide solution, but does show some swelling in 8% sodium hydroxide solution and in concentrated formic acid, and is soluble in 60% sulfuric acid, in concentrated hydrochloric acid (d 1.12) and in 78-97% phosphoric acid, which indicates the linear nature of the molecules in the substance.

A part of the obtained ether specimen (3 g) was etherified a second time under the same conditions and same ratio of substances as in the previous synthesis. After a second etherification the behavior of Specimen 1_1 toward solvents failed to change, although the degree of substitution was raised: $\Sigma OCH_2CHOHCH_2OH$ for Specimen 1 was 25.66, while for Specimen 1_1 it was 32.32. We will mention that a high degree of substitution was also achieved in that modification of the synthesis where the thoroughly pulverized chitin (0.25 mm screen) was made to swell in 43% sodium hydroxide under good vacuum for 5-10 hours, and where 300 ml of sodium hydroxide solution was taken for 20 g of chitin. The alkali chitin, squeezed to a 2.8-fold weight, was heated at 60° for 40 hours with glycerol monohydrin in acetone.

A part of the obtained Specimen 2 was subjected to a second treatment by the just given directions, beginning with the steeping of the prepared ether in the caustic. The same treatments were successively repeated a third and fourth time. In this manner Specimens 2, 2_1, 2_2 and 2_3 were obtained, in which the degree of substitution (percent of glycerol residues) gradually rose.

When compared with Specimen 2, the behavior of the obtained specimens (2_1, 2_2 and 2_3) toward water and other solvents was impaired. Thus, Specimen 2_2 was partially soluble in diluted acids – sulfuric (60%), concentrated hydrochloric and phosphoric (50-97%), while Specimen 2_3 was already insoluble in them, and proved to be completely nonswelling in alkalies. With repitition of the synthesis it can be seen that the number of "stitches" increased due to the presence of dichlorohydrin impurities. A positive influence on the solubility of the specimens, especially in acids, could have been exerted by the fact that in the repeated syntheses the number of free amino groups (deacetylated by the alkali) increased, but this failed to be shown.

TABLE 1

Specimen Nos.	% Glycerol Residues	% Acetyl Groups	%C	%H	%N
2	23.77	–	–	–	–
2_1	32.37	8.36	–	–	–
2_2	47.40	–	–	–	–
2_3	49.00	3.70	47.40	7.88	3.63

Analysis of the specimens revealed that the degree of etherification gradually increased from Specimen 2 to Specimen 2_3, as can be seen from Table 1.

Specimen 2_3, on the basis of its complete analysis, can be assigned the structure:

$$C_{11}H_{20.0}O_{7.25}N_{0.75}$$

or

$$[C_6H_7O_3(NHCOCH_3)_{0.25}(NH_2)_{0.5}(OH)_{0.5}(OCH_2CHOHCH_2OH)_{1.5}]_n.$$

2. Chitin Glycerol Ethers Based on Glycidic Alcohol

Glycidic alcohol was obtained from the monochlorohydrin in known manner [10] (in yields up to 70% when the amount of metallic sodium was increased) and had the following constants:

B. p. 56-57° (1-1.5 mm), n_D^{20} 1.4336, d_4^{20} 1.1370, MR_D 16.90; calc. 17.15.

Alkali chitin was prepared by soaking chitin in 30-43% sodium hydroxide solution at room temperature in vacuo for 12 hours, or the method of repeated alternate freezing and thawing of the caustic solution containing the pulverized chitin was used. The coefficient of squeezing was 3. The synthesis was run in the same manner as when the monochlorohydrin was used. Usually the synthesis conditions were: 4:1 molar ratio of glycidic alcohol to chitin, temperature 56°, time 12-30 hours, and in either acetone medium or without it.

The glycerol ethers of chitin, obtained using glycidic alcohol, always showed swelling in moderately and strongly diluted, acetic, formic, oxalic and levulinic acids, and even dissolved in them, not to mention the mineral acids, which are excellent solvents; at times they dissolved in 4 and 8% sodium hydroxide solution and even partially in water. For this reason it was necessary to remove the alkali, not by the usual washing with water, but by dialysis and electrodialysis, in which connection cellophane was used as the membrane.

The demineralized moist product, swollen in water and partially dissolved in it, was precipitated by the addition of acetone with constant stirring. Here a white, highly swollen precipitate was obtained as a friable clod. The substance was repeatedly treated with dry acetone, then with ethyl ether, and dried in a vacuum-oven without heat.

The moist white product was soft and slightly gummy, but after drying it could easily be ground to a powder in a mortar. The specimens, dried without heat, dissolved in 4-8% sodium hydroxide and in 3-50% acetic acid, showed strong swelling in water, glacial acetic acid, and in dilute and concentrated formic and levulinic acids, but in the case of overdrying they showed considerably poorer swelling. For the case of glycidic alcohol the syntheses gave specimens with a moderate amount of glycerol residues, ranging from 6 to 36.70%. A higher degree of etherification was achieved by making a second addition of the glycidic alcohol in the ratio of 4 moles of the alcohol to 1 mole of chitin. The total yields of the products reached 110% of the original chitin weight.

A comparison of the nitrogen and acetyl group analyses shows that there is considerable deacetylation of the amino groups under the influence of the alkali. From either the reaction mass or from the isolated product fractions could be obtained that differed in their solubility in both alkali and in 3-50% acetic acid.

The analyses for some of the obtained specimens are given in Table 2.

TABLE 2

Specimen Nos.	Synthesis conditions	Elementary composition (in %)			% Acetyl Groups CH_3CO	% Glycerol Residues $OCH_2CHOHCH_2OH$
		C	H	N		
3	Steeping of chitin in 43% alkali solution in vacuo. The glycidic alcohol was added three times in amounts of 4 moles, without adding alkali; the synthesis was run for 12 hours in acetone medium	46.20	7.43	4.81	4.67	42.45
4	The same as for Specimen 3, but the synthesis was run in acetone medium					
	Fraction 1	45.56	7.16	6.74	–	14.45
	Fraction 2	45.33	7.73	4.35	–	22.60
4_1	Before its isolation Specimen 4 was additionally treated with 4 moles of glycidic alcohol, 12 hours, 56°, in acetone	45.97	7.31	4.88	–	36.70

Both the preceding chitin glycerol ether specimens and the specimens based on glycidic alcohol were analyzed for their nitrogen content by the Dumas and Kjeldahl methods, in known manner [11] for the number of acetyl groups, while the number of glycerol radicals was determined by the Zeisel method. In all cases the average values of 2-3 parallel determinations are given.

Such glycerol ether specimens, even those with a low degree of substitution (with a glycerol radical content of 8.13, 13.25, 5.98 and 5.44%), showed swelling in glacial and 50% acetic acid, in different concentrations of formic acid, and dissolved in mineral acids. With a higher degree of etherification the specimens showed swelling in 4-8% sodium hydroxide and even in water, and became soluble in very dilute organic acids, which is characteristic for Specimens 3 and 4 (Table 2).

The composition for Specimens 3 can be shown by the formula.

$$C_{10.3}H_{18.9}O_{6.8}N_{0.9}$$

or

$$[C_6H_7O_2(NHCOCH_3)_{0.29}(NH_2)_{0.63}(OH)_{0.76}(OCH_2CHOHCH_2OH)_{1.24}]_n.$$

The glycerol ethers of chitin, dissolving in 4 and 8% sodium hydroxide, were characterized by their viscosities at 5 concentrations, ranging from 0.05 to 0.79 g/100 ml at 20 ± 0.01°. For Specimen 4 the characteristic viscosities were found to be, in 4% sodium hydroxide – 2.6, and in 8% sodium hydroxide – 2.4; for Specimen 4_1, Fraction 2, the corresponding values were 3.9 and 2.9. The proximity of the values of the characteristic viscosities for Specimens 4 and 4_1, combined with the proximity of their composition, speaks in favor of their molecular weights being close.

Although the chitin glycerol ethers, obtained through the glycidic alcohol, show considerable solubility, still the products of the syntheses are heterogeneous; we were unable to obtain specimens that were completely soluble in water or even in dilute caustic solution. In synthesizing the ethers considerable self-condensation of the glycidic alcohol under the influence of alkali and heat is observed.

SUMMARY

1. Glycerol ethers of chitin have been synthesized for the first time by the reaction of either glycerol monochlorohydrin or glycidic alcohol with chitin in the presence of alkali; deacetylation of the amino groups in chitin proceeds both during the time of preparing the chitin for reaction and in the synthesis itself.

2. The success of the synthesis depends on the use of thoroughly pulverized chitin and especially on the ability to achieve the highest possible degree of swelling in alkali by either the technique of repeated alternate freezing and thawing of the alkali solutions containing the chitin, or by the method of steeping the chiting under reduced pressure at room temperature.

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CHEMISTRY OF CHLOROMYCETIN (LEVOMYCETIN)

V. RACEMIZATION OF L-THREO-1-(p-NITROPHENYL)-2-(DICHLOROACETAMIDO)-1,3-PROPANEDIOL WITH SUBSEQUENT CONVERSION OF THE RACEMATE INTO CHLOROMYCETIN (LEVOMYCETIN) [1]

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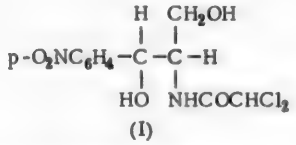
The chloromycetin molecule (levomycetin, chloroamphenicol), being D-threo-1-(p-nitrophenyl)-2-(dichloroacetamido)-1,3-propanediol (I), contains two asymmetric carbon atoms, as a result of which in the process of synthesizing this compound there can be formed, together with it,



(I)

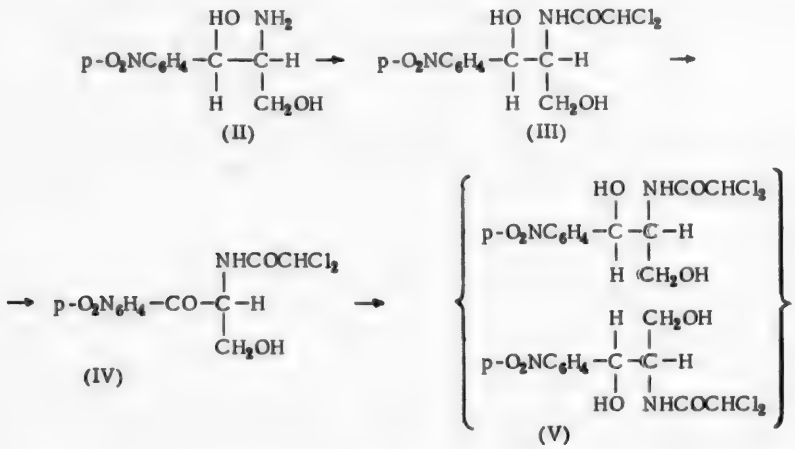
all three of its theoretically possible spatial isomers: L-threo-, D-erythro- and L-erythro-1-(p-nitrophenyl)-2-(dichloroacetamido)-1,3-propanediols. These three stereoisomers differ from chloromycetin in that for all practical purposes they are completely devoid of antibacterial, antirickettsial and antiviral activity, and in addition they show considerable toxicity. In connection with this, immediately after the structure and synthesis of chloromycetin had been elucidated, there arose two problems before the investigators: 1) to find rational methods for the separation of chloromycetin from its inactive and toxic stereoisomers, and 2) to elucidate the possibility of converting these stereoisomers into chloromycetin. The first of these problems was successfully solved by us as early as 1949 [2]; simultaneously and independent of our work the problem was solved by some American investigators, and later a number of methods were described in the literature for the separation of chloromycetin or its intermediate synthesis products from the corresponding compounds, possessing the D,L-erythro and L-threo configurations.* As regards the second problem, here until recently only a partial solution had been achieved – it was possible to realize only the isomerization of compounds of the erythro series into compounds of the threo series [3-5, 13, 14], while the question as to the possibility of racemizing compounds of the L-threo series remained unanswered. This question was recently solved by us, in which connection a brief summary of the performed work was published as a preliminary communication [15]. In this paper we describe the results of those investigations in more detail.

As is known [3, 4, 6-10], in the synthesis process for chloromycetin it is usually the intermediately formed D,L-threo-1-(p-nitrophenyl)-2-amino-1,3-propanediol that is subjected to separation into its optically active forms, and much less frequently the N-dichloroacetyl derivative of this compound (racemate of chloromycetin), obtaining thus as nonutilizable secondary products the L-threo-aminodiol (II) or, correspondingly, the L-threo-N-dichloroacetamidodiol (III). In elucidating the possibility for the direct racemization of compounds (II) and (III), and also of the azomethine and N,N,O-, and N,O,O-acyl derivatives of the first of them,** all we obtained were

* For more details of this cf. [3], where a summary of the literature published up to 1953 is presented; for data on later investigations cf. [4-12].

** Containing, in part, strongly electron-accepting groups like, for example, the 2,4-dinitrobenzylidene or 2,4-dinitrobenzoyl radicals.

negative results. In the treatment of all of these compounds with diverse acidic and basic substances, and also with many other reagents under various reaction medium and temperature conditions,* either racemization failed to proceed, or it was accompanied by very profound changes in the compounds being racemized. The difficultly for racemization of our investigated substances was, apparently, associated with the fact that in their molecules the groupings were absent, capable of essentially augmenting the mobility of the hydrogen atoms found at the asymmetric carbon atoms; consequently, it was decided to destroy one of the centers of asymmetry, at the same time creating a grouping that would facilitate racemization of the second center, and to combine the realization of the racemization process itself with the reduction of the first center of asymmetry. In accord with this we planned to convert the L-threo-aminodiol (II) into the L-threo isomer of chloromycetin (III), oxidize the secondary alcohol group in the latter to the carbonyl group, then subject the thus obtained optically active ketone (IV) to either sequential or simultaneous racemization and reduction, and finally end up with the racemate of chloromycetin (V).



A detailed study of these reactions revealed that the given path permits easy passage from the L-threo compounds (II) and (III) to the racemate of chloromycetin (V), and then to chloromycetin (I) itself. The first step of our studied transformations – the N-dichloroacetylation of the L-threo-aminodiol (II) – was realized with the aid of the methyl ester of dichloroacetic acid, which ester acylates only the amino group in amino alcohols. It follows that this reaction should be run under the conditions developed by us earlier for the synthesis of chloromycetin [2, 16], taking the methyl dichloroacetate in not more than 20% excess and heating the reaction mixture at 90-100° for not over 30 minutes, so as to avoid reducing the yield and impairing the quality of the formed L-threo isomer of chloromycetin (III). It is also expedient to run this process in the presence of isoamyl alcohol, gradually distilling off the methyl alcohol formed in the reaction. The latter has to be removed due to the excellent solubility of the obtained L-threo compound (III) in it, while the presence of the isoamyl alcohol is desirable for the reason that it is a good solvent for the secondary reaction products. When the above indicated conditions are observed the yield of the L-threo compound (III) reaches 90-93%, in which connection the substance is obtained in such high purity that its purification by recrystallization is superfluous. However, it is even more convenient to run the reaction for the dichloroacetylation of the L-threo-aminodiol (II) in isopropyl alcohol medium at the boiling point of the latter, with subsequent dilution of the reaction mixture with water. By this method the L-threo compound (III) is obtained in the same yield and with the same purity as in the above described procedure.

It should be mentioned that the methyl dichloroacetate, needed for the synthesis of the chloromycetin (I) and its stereoisomer (III), can easily be obtained by the reduction of trichloroacetic acid with zinc dust in methyl alcohol medium, in which connection the esterification of the formed dichloroacetic acid can be achieved without

* For example, the inorganic and organic acids (H_2SO_4, HCl, HPO_3, HCOOH etc.), their anhydrides and acid halides ($SOCl_2$, SO_2Cl_2, $POCl_3$, PCl_5, Ac_2O, AcCl etc.), bases (pyridine, quinoline, piperidine, N-ethylpiperidine, etc., alkali carbonates and hydroxides, alcoholates (lithium, sodium, potassium, aluminum), and the alkali and alkaline earth metals (Li, Na, K, Mg, Ca) in the presence or in the absence of various polar and nonpolar solvents.

its prior isolation by the method of boiling the reaction mixture with concentrated sulfuric acid. However, the dichloroacetic acid and its methyl ester, obtained both here and under the conditions described earlier in the literature [17], always contain small amounts of trichloroacetic and monochloroacetic acids or their esters, which cannot be completely removed by fractional distillation. The presence of these impurities even in traces sharply reduces both the quality and the yield of chloromycetin (I) and its stereoisomer (III).

So as to render the methyl ester of dichloroacetic acid completely free of the methyl esters of trichloroacetic and monochloroacetic acids, it proved necessary to: 1) use a slight excess (0.1 mole) of zinc dust in the reduction, which permits achieving the complete absence of the methyl ester of trichloroacetic acid in the obtained products; 2) heat the obtained products with pyridine, which makes it possible to completely remove the methyl ester of monochloroacetic acid. Under the conditions developed by us a 50% yield of pure methyl dichloroacetate is obtained.

The second step of our proposed method for the racemization of the L-threo-aminodiol (II) – the oxidation of the L-threo-N-dichloroacetamidodiol (III) to the corresponding optically active ketone (IV) – can be realized with the aid of either chromic anhydride or potassium permanganate. In the attempts to find the optimum conditions for the oxidation of compound (III) with chromic anhydride the influence on the process of the medium (water, acetone, acetic acid, sulfuric acid), the amount of oxidizing agent used (from 0.5 to 2 moles), the time of its addition (from 1.5 to 5.5 hours), and the temperature (from 45 to 105°), was studied; here it was established that independent of the oxidation conditions a part of the original compound (III) always remains unchanged, while another part is subjected to deeper oxidation clear up to p-nitrobenzoic acid, as a result of which the ketone (IV) is formed in low yield.* In addition, the oxidation with chromic anhydride proceeds slowly and is accompanied by the formation of tarry products, which make the isolation and purification of the ketone (IV) difficult. Even under the optimum conditions (cf. EXPERIMENTAL) the latter is obtained in yields not exceeding 25-27%.

The oxidation of compound (III) proceeds much better with potassium permanganate. In studying this reaction we varied widely the amount of oxidizing agent (from 100 to 300%), the amount of solvent and the nature of the medium, and also the temperature (from 0 to 45°). As a result it was established that the oxidation process should be run in acetic acid solution at 15-20°, taking a 1.5-fold amount of potassium permanganete, dissolved in 10% sulfuric acid. In this case the isolation of the ketone (IV) is realized very simply – after removal of the formed manganese dioxide by filtration the solution under cooling is neutralized with concentrated ammonia solution to pH 6-6.5, as a result of which all of the ketone (IV) precipitates from solution, here in such pure form that it can be used for subsequent transformations without additional purification. Here the yield of ketone (IV) is 50-53%, since independent of the oxidation conditions, the same as when chromic anhydride is used, a part of the original compound (III) always remains unchanged, while another part is oxidized to p-nitrobenzoic acid. The pure α-(dichloroacetamido)-β-hydroxy-p-nitropropiophenone (IV) has m. p. 124-125° (from benzene); $[\alpha]_D^{18} = -10.5°$ (c = 4 in C_2H_5OH). **

The third (last) step – the racemization and reduction of ketone (IV) – required especially detailed study. Here the simultaneous realization of both reactions proved to be the most desirable, i.e. the transformation of the ketone (IV) directly into the chloromycetin racemate (V). This we were able to achieve by running the process under the usual conditions for the Meerwein-Ponndorf reaction, using 1.5-2 moles of aluminum isopropylate in isopropyl alcohol medium. However, very pronounced tar formation was observed here, and in addition the reduction of the ketone (IV) proceeded at a faster rate than did its isomerization, as a result of which, together with the chloromycetin racemate (V), the original chloromycetin L-threo isomer (III) was formed in considerable amounts. Although increasing the amount of aluminum isopropylate to 5 moles led to some acceleration of the racemization process, still this acceleration was only slight. The addition of acetone, benzene and other substances to the reaction medium, which could have retarded the reduction process, failed to improve the situation. Sodium isopropylate proved to be a considerably more effective means, the addition of which in small,

* In order to have a means of evaluating the amounts of formed ketone (IV) and p-nitrobenzoic acid, and also of the unreacted L-threo-N-dichloroacetamidodiol (III), we developed a procedure for the separation and determination of the three mentioned compounds. The procedure consists in the extraction from the reaction mass (previously diluted with water) of the ketone (IV) and p-nitrobenzoic acid with dichloroethane, a solvent in which compound (III) is insoluble. The latter is then extracted with ether, while the ketone (IV) and p-nitrobenzoic acid are separated by means of soda solution.

** The properties of this compound and its antipode were briefly described by us earlier [18].

but strictly controlled amounts (0.14 mole), not only accelerated the racemization, but also sharply reduced the amount of tar formation. In the presence of the indicated amount of sodium isopropylate the amount of tar formation is extremely slight if the reaction is run at 60° for 6 hours, and is practically absent if the process is run at 37° for 24 hours. However, even under the last indicated most favorable conditions, the ketone (IV) succeeds in being partially reduced before it has a chance to be racemized, and consequently, together with the chloromycetin racemate (V), formed in about 45% yield, the chloromycetin L-threo isomer (III) is always obtained in 13-17% yield.* It should be mentioned that the separation of compound (V) from compound (III) is easily achieved with the aid of either ethyl acetate or dichloroethane, in which solvents compound (V) is considerably less soluble than is compound (III). The isolated racemate (V) can be used for subsequent conversion into the optically active chloromycetin (I) without additional purification by recrystallization.

Although methods for the direct conversion of the racemate (V) into the chloromycetin (I) are described in the literature [3, 12], still it is more advantageous to first hydrolyze the racemate to D,L-threo-1-(p-nitrophenyl)-2-amino-1,3-propanediol, separate the latter into its antipodes, and then convert the isolated D-threo isomer into the chloromycetin (I). According to our data, the hydrolysis of the racemate (V) proceeds in 90% yield under the conditions of boiling it for 1 hour with 20% hydrochloric acid. Of the methods known at the present time for the separation of D,L-threo-1-(p-nitrophenyl-2-amino-1,3-propanediol into its antipodes and the conversion of the D-isomer into chloromycetin (I) [2-4, 6-10, 16], our method [2, 16], described in detail in the EXPERIMENTAL, remains one of the most successful, which with the acid of d-tartaric acid permits the rapid separation of the racemic aminodiol into its antipodes and then further permits the isolation of each of the antipodes in yields reaching 80-82%;** the subsequent N-dichloroacetylation of the D-antipode makes it possible to easily obtain chloromycetin (I) in 90-93% yield, since the L-antipode can again be subjected to racemization.

As a result, the studies made by us permitted solving for the first time the problem of converting the biologically inactive L-threo isomer (III) of chloromycetin into its active D-threo form (I).

EXPERIMENTAL

1. Preparation of Methyl Dichloroacetate

To 409 g (2.5 moles) of trichloroacetic acid in 0.5 liter of methyl alcohol with vigorous stirring was gradually added 200 g of 90% zinc dust (2.75 moles). The zinc dust was added over 2-3 hours, taking care that the temperature of the reaction mass was kept at 10-20°. Then the temperature was raised to 30° and the reaction mass was stirred at this temperature for 0.5 hour. After this the mixture was cooled to 15-20°, and the small amount of precipitate was filtered and washed in two portions with 50 ml of methyl alcohol. To the filtrate, containing dichloroacetic acid and zinc chloride, was gradually added 130 ml of concentrated sulfuric acid, in which connection the reaction mixture heated up strongly and at the same time a copious precipitate of zinc sulfate began to separate. After all of the sulfuric acid had been added the reaction mixture was boiled for 15 minutes, then cooled to 15-20°, and the thick mass poured into a mixture of 3.5 liters of water and 1 kg of ice. The resulting oil was separated and washed with water, then with 130 ml of 2% sodium bicarbonate solution and again with water, after which 10 g of anhydrous calcium chloride was added, which was removed by filtration after 2 hours. The yield of the methyl dichloroacetate was about 270 g, which was purified as follows. The ester was heated to 95° and to it was gradually added with stirring 27 g of dry pyridine, after which the reaction mixture was heated at 95-100° for 1 hour. The mass darkened rapidly and toward the end of heating had become brown. On conclusion of heating the reaction mass was cooled to 15-20°, acidified under stirring with 10% sulfuric acid until it showed acid to Congo, and then the mixture was steam-distilled. The lower distillate layer was separated and washed with 10% sulfuric acid, 2% sodium bicarbonate solution, and finally with water. The obtained methyl dichloroacetate was dried for a day over 27 g of anhydrous calcium chloride and then vacuum-distilled, collecting the fraction with b. p. 73-76° at 68-70 mm. Weight 186 g; yield 52%.

* An attempt was made to divide the process into two stages – to first realize racemization, and then reduction of the ketone (IV). The racemization was run for 3-6 hours at 55-65° in different solvents (anhydrous isopropyl alcohol, acetone, benzene) and in the presence of sodium ethylate (from 0.14 to 1.4 moles) or aluminum isopropylate (from 0.25 to 5.2 moles), but in all of these cases less satisfactory results were obtained than those given above.

** The separation of the racemate is easily achieved due to the difference in the solubilities of the acid d-tartrates of D- and L-threo-1-(p-nitrophenyl)-2-amino-1,3-propanediol in methyl alcohol and in water (the d,L-salt is more soluble than the d,D-salt), and due to the ability of the d,L-salt to form quite stable supersaturated solutions.

2. Preparation of L-threo-1-(p-Nitrophenyl)-2-(dichloroacetamido)-1,3-propanediol (III)

a) A mixture of 25 g of L-threo-1-(p-nitrophenyl)-2-amino-1,3-propanediol (II), 15 ml of methyl dichloroacetate and 13 ml of dry isoamyl alcohol was heated with stirring to 84-86°. At this temperature the methyl alcohol, formed as the result of reaction, began to distill. In measure with removal of methyl alcohol by distillation the temperature of the mass gradually rose to 100-102°. After 20 minutes from the beginning of methyl alcohol distillation the reaction mixture was cooled to 95° and seeded. Crystallization began rapidly, the heat of which caused the temperature of the mass to again rise to 100-102°; at the same time some more methyl alcohol distilled (a total of 4.5-5 ml). Continuing the cooling, the temperature of the reaction mass was reduced to 40-50°. The still warm mass was rubbed, cooled to 15-20°, and allowed to stand at this temperature for 1 hour, after which the precipitate was transferred to a filter, pressed well, washed 3 times with dry dichloroethane (taking it in 17 ml portions) and, finally, 2-3 times with ice water. The obtained L-threo-1-(p-nitrophenyl-2-(dichloroacetamide)-1,3-propanediol (III) was dried at 50-70°. Weight 34.7 g (91%). M. p. 149-151°; $[\alpha]_D^{25} = -18.5°$ (c = 4.9 in C_2H_5OH).

b) A mixture of 20 g of the pure L-threo-1-(p-nitrophenyl)-2-amino-1,3-propanediol (II), 13 ml of methyl dichloroacetate and 13 ml of anhydrous isopropyl alcohol was boiled under stirring for 1 hour; here the precipitate dissolved at first, but after some time a crystalline substance separated. The reaction mass was cooled to 75° and, adding to it 43 ml of water heated to 70-75°, again heated to the boil to dissolve the obtained precipitate. Then the solution was cooled to 60°, seeded, and the cooling contained down to 5°. At this temperature the reaction mass was stirred for an hour, after which the obtained precipitate was filtered, pressed well, first washed twice with 25% isopropyl alcohol, then 3-4 times with dichloroethane (each time taking 10 ml portions of the indicated solvents, cooled to 5°), and finally with ice water. The obtained L-threo-1-(p-nitrophenyl-2-(dichloroacetamido)-1,3-propanediol (III) was dried at 50-70°. Weignt 27.9 g (91.5%). M. p. 149-151°; $[\alpha]_D^{25} = -18.6°$ (c = 4.9 in C_2H_5OH).

3. Preparation of α-(Dichloroacetamido)-β-hydroxy-p-nitropropiophanone (IV)

a) To a solution of 30 g of L-threo-1-(p-nitrophenyl)-2-(dichloroacetamido)-1,3-propanediol (III) in 300 ml of glacial acetic acid under constant stirring was added over 45 minutes a solution of 14.6 g of potassium permanganate in 225 ml of 10% sulfuric acid, taking care that the temperature of the reaction mass was kept at 15-20°. After all of the oxidizing agent had been added the stirring was continued for another 15 minutes, then 300 ml of water was added, and the mixture kept at 15-20° for 30 minutes without stirring. The obtained manganese dioxide precipitate was filtered and washed 3 times with water, each time taken in 15 ml portions. The completely clear, almost colorless, filtrate was combined with the wash waters and then cooled to 5°, where the ketone (IV) usually began to precipitate. To the cooled reaction mixture at 5-10° and vigorous stirring was added over 2-3 hours a concentrated aqueous ammonia solution. The amount of precipitated ketone (IV) quickly increased. The addition of ammonia was continued to a pH of 6-6.5 (by Universal indicator), for which about 400 ml of ammonia solution was required. The reaction mass was cooled to −3° and held at this temperature for 30 minutes. The resulting ketone (IV) (precipitate) was filtered, pressed, and washed with ice water until sulfate ions were absent in the filtering. The well pressed precipitate was vacuum-dired at 25-35°. There was obtained 15.6 g of α-(dichloroacetamido)-β-hydroxy-p-nitropropiophenone (IV). Yield 52%. M. p. 117-121°.

b) To a mixture of 30 g of L-threo-1-(p-nitrophenyl)-2-(dichloroacetamido)-1,3-propanediol (III), 90 ml of dichloroethane and 30 ml of glacial acetic acid was added over 6 hours with constant stirring a solution of 15 g of chromic anhydride in 30 ml of water, the temperature of the reaction mixture being maintained at 40-45°. As the oxidizing agent was added, the precipitate of the L-threo compound (III) gradually dissolved. After all of the chromic anhydride had been added the reaction solution was held at 40-45° for 1 hour, after which it was poured into 450 ml of water, and then extracted 5 times with dichloroethane, taking the latter in 150 ml portions. The thus obtained dichloroethane solution was washed 2-3 times with 10% aqueous soda solution and then with water, after which the dichloroethane was removed by distillation (at the end in vacuo). The oily residue was boiled for 30 minutes with 60 ml of chloroform and, having cooled the mixture to 5°, held at this temperature for 1 hour, after which the precipitate was filtered and washed with 10 ml of chloroform. This operation was repeated twice, each time heating the precipitate with 20 ml of chloroform and taking the latter in 5 ml portions for washing. There was obtained 8.1 g of α-(dichloroacetamido)-β-hydroxy-p-nitropropiophenone (IV) with m. p. 117-121°. Yield 27%.

4. Preparation of D,L-Threo-1-(p-nitrophenyl)-2-(dichloroacetamido)-1,3-propanediol (V)

To a hot solution of 50 g of aluminum isopropylate in 130 ml of anhydrous isopropyl alcohol was added a solution of sodium isopropylate, prepared by dissolving 0.15 g of metallic sodium in 26 ml of boiling anhydrous isopropyl alcohol, containing 0.8 g of aluminum isopropylate. The mixture, having been boiled for 5-10 minutes, was cooled to 60° and with vigorous stirring to it was gradually added 15.6 g of α-(dichloroacetamido)-β-hydroxy-p-nitropropiophenone (IV) with m. p. 117-121°, after which stirring of the reaction mass was continued at 60° for 6 hours. On conclusion of this to the orange solution with strong stirring and temperature not exceeding 60° was added a solution of 0.8 g of concentrated sulfuric acid in 45 ml of water; here a yellow precipitate was obtained. The reaction mass was boiled for 1 hour, after which it was filtered hot. The precipitate was broken up, boiled under stirring for 30 minutes with 150 ml of 80% isopropyl alcohol, and filtered hot. This operation was repeated twice more with new portions of 80% isopropyl alcohol, taking it each time in 150 ml portions. The reaction solution and the filtrate from the first extraction were combined and boiled for 30 minutes with 2 g of activated charcoal. The charcoal was filtered and washed with 20 ml of hot 80% isopropyl alcohol. The obtained filtrate, wash alcohol, and filtrates from the second and third extractions were combined and evaporated to dryness in vacuo at a bath temperature of 60-70°. The residue was crushed, treated with 15 ml of ethyl acetate and boiled for 30 minutes, after which it was cooled to 0° and kept at this temperature for 2 hours. The precipitate was filtered and washed, first in three doeses with 9 ml of ethyl acetate cooled to 0-2°, then in three doses with 12 ml of dichloroethane cooled to 0-2 °, and finally with ice water. This gave 7.1 g (45%) of D,L-threo-1-(p-nitrophenyl)-2-(dichloroacetamido)-1,3-propanediol (V) with m. p. 149-151°; after recrystallization from isoamyl alcohol the m. p. was 152-152°.

All of the ethyl acetate and dichloroacetane solutions were combined and evaporated in vacuo to dryness. To the obtained oily residue was added 12-15 ml of dichloroethane, the mixture allowed to stand for 1 hour at 12-15°, and the separated precipitate filtered. Recrystallization from water with the use of activated charcoal gave 2.0 g (13%) of L-threo-1-(p-nitrophenyl-2-(dichloroacetamido)-1,3-propanediol (III) with m. p. 151-152°.

5. Preparation of D,L-Threo-1-(p-nitrophenyl)-2-amino-1,3-propanediol

A mixture of 10 g of the D,L-threo-1-(p-nitrophenyl)-2-(dichloroacetamido)-1,3-propanediol (V) obtained in Experiment 4, with m. p. 149-151°, and 20 ml of 20% hydrochloric acid was boiled for 1 hour, after which the obtained solution was cooled to 5° and kept at this temperature for 2 hours. The resulting hydrochloride (precipitate) was filtered and washed on the filter 3 times with dichloroethane, the latter being taken in 3 ml portions each time (cf. [19]). The precipitate was dissolved with heating in 20 ml of water, 0.3 g of activated charcoal added, the mixture boiled 10 minutes, filtered, and to the filtrate, cooled to 15-20°, was added with stirring 10% aqueous sodium hydroxide solution to pH 10-10.5; about 22 ml of alkali solution was required. After 2 hours at 10-15° the precipitate was filtered and washed 2-3 times with ice water, taking it each time in 3-5 ml portions, weight 5.9 g (90%). The obtained D,L-threo-1-(p-nitrophenyl)2-amino-1,3-propanediol had m. p. 140-142°.

6. Separation of D,L-Threo-1-(p-nitrophenyl)-2-amino-1,3-propanediol Into Its Antipodes

a) Thirty grams of D,L-threo-1-(p-nitrophenyl)-2-amino-1,3-propanediol was dissolved in 270 ml of boiling methyl alcohol and to this solution was added at one time under stirring 26.5 g (25% excess) of well pulverized d-tartaric acid. A mixture of the acid d-tartrates of the D- and L-threo-1-(p-nitrophenyl)-2-amino-1,3-propanediols quickly precipitated from the solution. The reaction mass was boiled for 1 hour, then cooled to 20°, and stirred at this temperature for another hour. The precipitate was filtered and washed twice with methyl alcohol, taking the latter in 15 ml portions for each washing.

The obtained cake of mixed salts was boiled under stirring with 500 ml of methyl alcohol for 1.5 hours, cooled to 20°, and the stirring continued at this temperature for 30 minutes. The precipitate was filtered and washed 3 times with methyl alcohol, taking the latter in 15 ml portions for each washing. The decomposition temperature of the salt was 182-184°. The well pressed cake was extracted a second time under the same conditions with 150 ml of methyl alcohol. After cooling, filtration, and washing with methyl alcohol (3 times with 10 ml portions) the pure acid d-tartrate of D-threo-1-(p-nitrophenyl)-2-amino-1,3-propanediol was obtained with

m. p. 186-187° (decompn). Weight 23.6 g (92%).*

The obtained salt was dissolved at 60-70° in 240 ml of water, 0.4 g of activated charcoal added to the solution, the hot solution stirred for 10 minutes, and the charcoal filtered and washed on the filter with 20 ml of hot water. The filtrate, combined with the wash waters, was cooled (usually the salt begins to crystallize here) and with stirring a concentrated aqueous ammonia solution was added slowly, taking care that the temperature of the mixture did not rise above 20°. Here the salt dissolved completely at first, and then the amine began to separate. The ammonia addition was terminated when distinct alkaline reaction to phenolphthalein was reached, for which about 13 ml of 25% aqueous ammonia solution was required. Then the reaction mixture was cooled to 10° and stirred at this temperature for 2 hours, periodically checking for alkalinity of the medium. The resulting precipitate was filtered and washed twice with ice water, taken each time in 10 ml portions. The obtained D-threo-1-(p-nitrophenyl)-2-amino-1,3-propanediol was first dried at 50-60°, and at the end at 70-80°. Weight 12 g, which represents an 87% yield, based on bitratrate taken for the decomposition, or 80%, based on the D-threo-aminodiol contained in the original racemic amine. M. p. 161-162°.**

b) In 75 ml of water at 85° was successively dissolved under stirring 30 g of D,L-threo-1-(p-nitrophenyl)-2-amino-1,3-propanediol and 26.5 g of d-tartartic acid. The reaction solution was heated at 70° for 1 hour, after which it was cooled to 60° and 150 ml of methyl alcohol was added. The acid d-tartrates of the D- and L-threo-aminodiols separated on cooling to 0°. For more complete crystallization of these salts the reaction mixture was kept at 0° for 1 hour. The thick slurry was again heated to 45-50° and then stirred at this temperature for 30 minutes, where the bitratrates of the L-threo-aminodiol was preferentially dissolved. The undissolved precipitate was filtered on a previously heated Buchner funnel, washing the reaction flask with the mother liquor, warmed to 45-50°. The precipitate was washed in three doses with 65 ml of methyl alcohol and dried. Weight 27 g; m. p. 178-182° (decompn). The obtained salt was crushed well and boiled with 150 ml of methyl alcohol for 1 hour, after which the mass was cooled to 10° and stirred at this temperature for another hour. The precipitate of the acid d-tartrate of D-threo-1-(p-nitrophenyl)-2-amino-1,3-propanediol was filtered and washed in two doses with 45 ml of methyl alcohol; Weight 23.2 g (90.5%); m. p. 186-187° (decompn).*** The D-threo-1-(p-nitrophenyl)-2-amino-1,3-propanediol is isolated from the obtained salt by the method described in Experiment 6a.

c) To isolate the L-threo-1-(p-nitrophenyl-2-amino-1,3-propanediol (II), all of the mother liquors obtained in Experiment 6a and 6b and containing the acid d-tartrate of this amine, a small amount of the acid d-tartrate of the corresponding racemate, and also some d-tartaric acid, were evaporated in vacuo. The residue, a viscous light-brown mass, was dissolved at 70° in 180 ml of water and, having added 1 g of activated charcoal to the hot solution, was stirred for 10-15 minutes, after which it was filtered. The charcoal was washed on the filter with 25 ml of hot water. The filtrate together with the wash waters was cooled to 20° and the L-threo-1-(p-nitrophenyl)-2-amino-1,3-propanediol (II) precipitated with ammonia under the conditions described for the isolation of the D-threo isomer (cf. Experiment 6a). The yield of the L-threo-aminodiol (II) was 12-13 g, with the corresponding racemate and ammonium tartrate being present as impurities. The L-threo-1-(p-nitrophenyl)-2-amino-1,3-propanediol with m. p. 163-164° can be obtained pure by recrystallization from water. However, for realizing the above described racemization of the L-threo-aminodiol (II) in Experiments 2, 3, and 4 this purification is superfluous, since the ammonium acid tartrate is easily separated at the stage of N-dichloroacetylation of the amine (Experiment 2); while the racemic amine in general cannot disturb the process; to be sure, it is necessary to keep in mind that the presence of the racemate does not permit controlling the purity of the obtained intermediate products by their constants.

7. Preparation of D-Threo-1-(p-nitrophenyl)-2-(dichloroacetamido)-1,3-propanediol (Chloromycetin, Levomycetin (I)

The dichloroacetylation of the D-threo-1-(p-nitrophenyl)-2-amino-1,3-propanediol should be run under the same conditions as described in Experiment 2. If the starting D-threo-aminodiol does not melt below 161°, then the

* If the decomposition temperature of the salt proves to be below 186° after the second extraction, then the cake should be subjected to a third extraction with 65 ml of methyl alcohol under the same conditions. Three washings with methyl alcohol are made, each time with 8 ml portions.

** If the melting point of the obtained amine is lower than the indicated, but not below 158°, then the amine should be stirred for 2 hours at 20° with a 12-fold amount of water. If the melting point of the amine is even lower, then it becomes necessary to recrystallize the amine from water.

*** If the isolated salt has a decomposition temperature lower than 186-187°, then, as in Experiment 6a, it should be given another extraction with 65 ml of methyl alcohol.

isolated chloromycetin has m. p. 149-151° and $[\alpha]_D^{25} = +18.5° (\pm 0.5°)$ (c = 4.9 in C_2H_5OH). It satisfies its assignment pharmacopoeia requirements and its additional purification by recrystallization is superfluous. The yield of the chloromycetin reaches 90-93%.

SUMMARY

The racemization of L-threo-1-(p-nitrophenyl)-2-(dichloroacetamido)-1,3-propanediol and subsequent conversion of the obtained racemate into chloromycetin (levomycetin) were realized.

The racemization of the L-threo-1-(p-nitrophenyl)-2-(dichloroacetamido)-1,3-propanediol proved possible only after one of the centers of asymmetry in the molecule was destroyed, with the simultaneous introduction of a grouping that facilitated the racemization of the second center; the latter process was run simultaneously with the reduction of the first center of asymmetry. In accord with what has been said the L-threo-1-(p-nitrophenyl)-2-amino-1,3-propanediol, obtained as a nonusable by-product in the synthesis of chloromycetin, was converted by heating with methyl dichloroacetate into L-threo-1-(p-nitrophenyl-2-(dichloroacetamido)-1,3-propanediol, and the latter was oxidized with potassium permanganate (or chromic acid) to the optically active α-(dichloroacetamido)-β-hydroxy-p-nitropropiophenone, which was then subjected to simultaneous racemization and reduction with the aid of aluminum and sodium isopropylates in isopropyl alcohol medium. The subsequent conversion of the obtained D,L-threo-1-(p-nitrophenyl)-2-(dichloroacetamido)-1,3-propanediol into chloromycetin was realized by the method of its hydrolysis to D,L-threo-1-(p-nitrophenyl)-2-amino-1,3-propanediol, which was then separated into its antipodes through the acid d-tartrates, while the isolated D-threo osomer was subjected to N-dichloroacetylation by heating it with methyl dichloroacetate.

As a result, for the first time the problem of converting its biologically inactive L-threo isomer into chloromycetin was volved.

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THE MIGRATION OF THE PEPTIDE RESIDUE IN PEPTIDE OF SERINE

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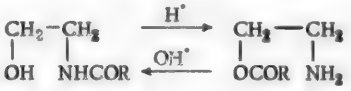
One of the specific characteristics of the acyl derivatives of amino alcohols and hydroxy amino acids, having the hydroxy and amino groups in vicinal position, is the ability of the acyl residue to migrate from the nitrogen to the oxygen, and from the oxygen to the nitrogen.

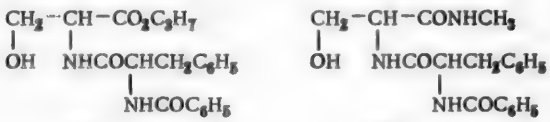


This reaction, studied in detail by a large number of investigators [1], attracted special attention recently, since the O-acyl derivatives of the alkanolamines have found wide use in medicine [2].

Recently, on the example of ethanolamine we showed that similar migration can proceed not only with the acyl, but also with the peptide (aminoacyl) residue [3].

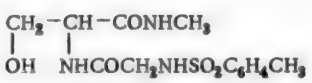
In the present work experiments were performed on the migration of the aminoacyl residue in the peptides of serine and its derivatives. A study of such reactions for serine peptides is of interest in connection with the investigation of the specific properties of the β-hydroxy amino acids. In recent years a number of studies have appeared, in which the migration of the peptide residue in the peptides of hydroxy amino acids during the time of acid hydrolysis of proteins was demonstrated [4].

The study subjects in the present work were the isopropyl ester of N-(N-benzoyl-3-phenylalanyl)serine (I), the methylamide of N-(N-benzoyl-3-phenylalanyl)serine (II), and the methylamide of N-(N-(p-toluenesulfonyl)glycyl] serine (III): [6].



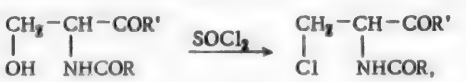
(I)

(II)

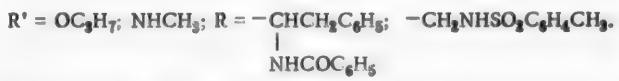


(III)

The experiments on the migration of the aminoacyl residue were run with the aid of thionyl chloride, with hydrogen chloride in either alcohol or dioxane solution, and with phosphorus pentachloride. Here the serine peptides were converted into derivatives of β-chloroalanine:



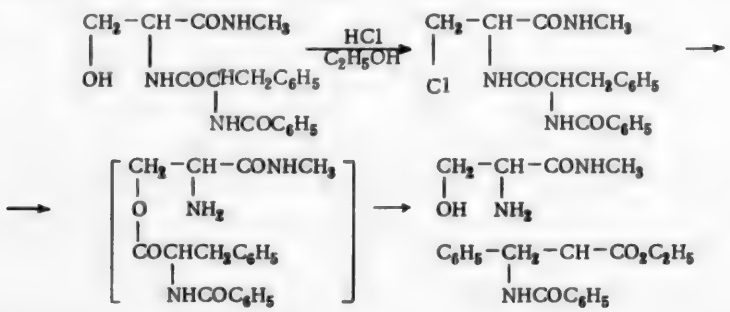
where



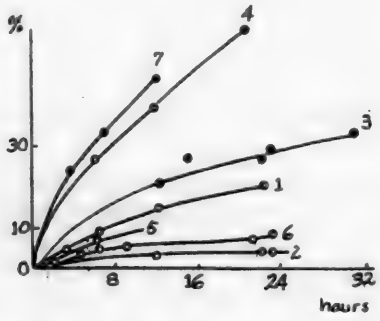
In not a single instance could the presence of oxazoline derivatives be revealed. As a result, the esters and amides of the acylated serine peptides behaved the same as the ethanolamine derivative: as the result of reaction there arose the β-chloro derivatives of amino acids. However, in contrast to the aminoacyl derivatives of

β-chloroethylamine, which are readily converted under the influence of water into the O-peptides of ethanolamine, the β-chloro derivatives of the peptides of alanine are saponified under these conditions to the starting serine peptides. Thus, the heating of the isopropyl ester of N-(N-benzoyl-3-phenylalanyl)-β-chloroalanine for 2 hours with aqueous dioxane gave the isopropyl ester of N-(N-benzoyl-3-phenylalanyl)serine, while the heating of the methylamide of N-(N-benzoyl-3-phenylalanyl)-β-chloroalanine with 50% alcohol gave the methylamide of N-(N-benzoyl-3-phenylalanyl)serine. In both cases the presence of amino nitrogen in the reaction solution could not be revealed; these facts are evidence that the peptide residue failed to migrate.

When the methylamide of N-(N-benzoyl-3-phenylalanyl)serine was treated with hydrogen chloride in anhydrous alcohol the main reaction products were the methylamide of N-(N-benzoyl-3-phenylalanyl)-β-chloroalanine and the ethyl ester of N-benzoyl-3-phenylalanine. Apparently, in this case the unstable methylamide of O-(N-benzoyl-3-phenylalanyl)serine is formed, which under the influence of the alcohol decomposes with the formation of the ethyl ester of N-benzoyl-3-phenylalanine:



The migration of the aminoacyl residue was qualitatively shown under the influence of conc. HCl on N-(N-acetyl-3-phenylalanyl)serine. Here the appearance of the hydroxamic reaction is distinct, which testifies to the formation of the ester bond. The resulting O-peptide is very unstable. The peptide is preponderantly hydrolyzed to serine and the acylated amino acid. Thus, 26-28% of the amino groups are liberated when the isopropyl ester of N-(N-benzoyl-3-phenylalanyl)serine is treated with conc. HCl, of which 72% belongs to serine. A somewhat indirect indication that the aminoacyl residue migrates under the influence of HCl is the difference in the hydrolysis rate of the N-peptides and N,O-peptides of serine. Under the influence of conc. HCl the N-(N-acetyl-3-phenylalanyl)serine hydrolyzes twice as fast as the N,O-bis(N-acetyl-3-phenylalanyl)serine. This difference is even sharper for the isopropyl esters of N-(N-phthaloylglycyl)serine and N,O-bis(N-phthaloylglycyl) serine (see Figure).



1) N-(N-acetyl-3-phenylalanyl)serine at 18°, 2) N,O-bis (N-acetyl-3-phenylalanyl)serine at 18°, 3) N-(N-phthaloylglycyl)serine isopropyl ester at 18°, 4) N-(N-phthaloylglycyl)serine isopropyl ester at 26°, 5) N,O-bis(N-phthaloylglycyl)serine isopropyl ester at 18°, 6) N,O-bis(N-phthaloylglycyl)serine isopropyl ester at 26°, 7) N-(N-benzoyl-3-phenylalanyl)serine isopropyl ester at 26°.

It is possible that the greater ease of hydrolysis of the serine N-peptides when compared with the N,O-peptides is due to prior migration of the peptide residue. Such migration, characteristic for the N-acyl derivatives of serine, cannot occur for the N,O-diacyl derivatives of hydroxyl amino acids. If the postulation is valid that the hydrolysis proceeds through the O-peptide stage, then the exclusion of water from the reaction mixture may facilitate the catching of the O-peptide. For this purpose a number of experiments were made with sulfuric acid; here we were able to realize migration of the peptide residue; the rearrangement was established indirectly by the change in the amount of amino nitrogen in the peptide solution. Having determined the amount of amino nitrogen in the peptide solution after its treatment with sulfuric acid, and then after the action of alkali on the acid solution, it becomes possible to establish the degree of migration of the peptide residue from the nitrogen to oxygen and from oxygen to nitrogen. The isopropyl ester of N-(N-benzoyl-3-phenylalanyl)serine, the methylamide of N-(N-benzoyl-3-phenylalanyl)serine and the methylamide of N-[N-(p-toluenesulfonyl)glycyl] serine were treated with sulfuric acid, and the amounts of

TABLE 1

Name of Substance	Reagent	Time	Temperature	Amino Nitrogen* (in %)		Migration (in %)
				after treatment with acid	after treatment with alkali	
N-(N-Benzoyl-3-phenylalanyl)serine isopropyl ester	Oleum	2 min.	50°	50	25	50
	Oleum	2 days	18	42	25	40
	100% H_2SO_4	10 min.	50	23	17	26
	100% H_2SO_4	3 hours	50	78	43	45
	100% H_2SO_4	3 days	18	41	26	37
N-(N-Benzoyl-3-phenylalanyl)serine methylamide	0.14 N Sulfuric acid in dioxane	1 hour	50	106	68	38
		1 hour	100	70	33	53
		2 hours	100	65	30	54
N-[N-(p-Toluenesulfonyl)glycyl] serine methylamide		1.5 hours	100	50	6	88
		2.5 hours	100	70	37	47

amino nitrogen and serine in the solution determined. An aliquot portion of the solution was treated with alkali, and the amount of amino nitrogen in the solution again determined. The determination results are given in Table 1. From the obtained results it follows that under the influence of sulfuric acid on serine derivatives the appearance of amino nitrogen is observed in all cases. The peptide solutions that were treated with sulfuric acid failed to contain serine, but gave a positive reaction for pyrotartaric acid and the double bond. These facts indicate that the migration reaction under the influence of sulfuric acid is not accompanied by hydrolysis of the peptides, but that together with the formation of the O-peptide there occurs dehydration and the appearance of aminoacrylic acid derivatives. It was established by means of special experiments that under the conditions for the Van Slyke determination of amino nitrogen the acyl derivatives of aminoacrylic acid are decomposed with the evolution of nitrogen; consequently, the measure of the number of amino groups, appearing as the result of the peptide residue migrating from nitrogen to oxygen, is only the difference between the determination of amino nitrogen in the solution before and after its treatment with alkali. The percent migration of the peptide residue from nitrogen to oxygen is calculated in the last column of Table 1. In not a single case did the migration reach 100% and it depended on the character of treating the peptide with sulfuric acid. The process went to greatest completion in the experiments with 0.14 N sulfuric acid in dioxane. Under the influence of the acid there was revealed 50% of the amino groups, which vanished nearly 100% after treatment with alkali. The degree of conversion of the N-peptide into the O-peptide was 88%. Apparently, the migration is accompanied by side reactions, which, probably, are not limited to the one phenomenon of dehydration. It should be mentioned that in the experiments performed by Desnuelle on proteins, the migration also failed to be complete.

When the present investigation had already been completed, there appeared in print the work of Elliott, in which the author effected the migration of the peptide residues in silk fibroin with the aid of H_2SO_4, and established that the migration of the peptide residue proceeds to the extent of 61%. In this manner the results, obtained by us on the peptides of serine, by Elliott on silk fibroin, and earlier by Desnuelle [4] on a number of other proteins, all established the ability for migration of the peptide residue under the influence of sulfuric and hydrochloric acids. However, these results should be regarded as being preliminary. They give a qualitative picture of the migration process, which undoubtedly is accompanied by a number of secondary processes.

EXPERIMENTAL

Conversion of the N-Peptide Derivatives of Serine Into the N-Peptide Derivatives of β-Chloroalanine

* The amino nitrogen, corresponding to the complete conversion of the N-peptide into the O-peptide, was taken as 100%.

TABLE 2

Weight (in g) *	Reaction conditions		Amino nitrogen (in %) **
	Time (in hrs.)	Temperature	
N-(N-Acetyl-3-phenylalanyl) serine			
0.0334	3	18°	4.5
0.0305	6	18	8.0
0.0296	12	18	14
0.0317	24	18	18.7
N,O-Bis(N-acetyl-3-phenylalanyl)serine			
0.0311	3	18	2.5
0.0533	6	18	3.9
0.0556	9	18	5.0
N-(N-Phthaloylglycyl)serine Isopropyl Ester			
0.0227	2	18	–
0.0282	12	18	20.5
0.0305	22	18	25
0.0311	31	18	32
0.0299	6	26	26
0.0325	12	26	38
0.0251	23	26	58
N,O-Bis(N-phthaloylglycyl)serine Isopropyl Ester			
0.0162	23	18	3.6
0.01665	6	26	6
0.0310	21	26	6.3
0.0250	23	26	7.4
N-(N-Benzoyl-3-phenylalanyl)serine Isopropyl Ester			
0.0256	4	26	28
0.0469	7	26	33
0.0439	12	26	46

* The weight corresponds to the aliquot portion taken for determination of the amino nitrogen.

** The amino nitrogen, formed in the hydrolysis of the peptide group, is taken as 100%.

N-(N-Benzoyl-3-phenylalanyl)-β-chloroalanine Isopropyl Ester.

a) A mixture of 0.5 g of the isopropyl ester of N-(N-benzoyl-3-phenylalanyl) serine (m. p. 168°) and 5 ml of thionyl chloride was heated at the boil for 3 minutes. Dilution of the reaction mixture with anhydrous ether gave crystals of the isopropyl ester of N-(N-benzoyl-3-phenylalanyl)-β-chloroalanine. M. p. 157°. The substance is unknown in the literature.

Found %: C 62.42, 62.33; H 6.11, 6.03; N 6.59, 6.66; Cl 9.16, 9.07. $C_{22}H_{25}O_4N_2Cl$. Calculated %: C 62.46; H 6.01; N 6.73; Cl 8.52.

b) Hydrogen chloride gas was passed for 2 hours into a solution of the isopropyl ester of N-(N-benzoyl-3-phenylalanyl)-serine in anhydrous dioxane. Dilution with water gave a precipitate of the isopropyl ester of N-(N-benzoyl-3-phenylalanyl)-β-chloroalanine. M. p. 155°. Its mixed melting point with the compound obtained in the preceding experiment failed to be depressed.

The isopropyl ester of N-(N-benzoyl-3-phenylalanyl)-β-chloroalanine was heated for 2 hours in aqueous-dioxane solution. Dilution of the reaction mass with water gave crystals of the isopropyl ester of N-(N-benzoyl-3-phenylalanyl)serine. M. p. 168°.. Its mixed melting point with the earlier obtained isopropyl ester of N-(N-benzoyl-3-phenylalanyl)serine failed to be depressed. The amount of amino nitrogen was determined by the Van Slyke method in an aliquot portion of the solution, while the amount of hydrochloric acid was determined by titration.

Found %: amino nitrogen 6, 4, 5. Calculated %: 100 (calculated on the basis of complete convertion of the N-peptide into the O-peptide).

0.0838 g substance: consumed 2.05 ml of 0.1 N NaOH; 0.1525 g substance: consumed 3.40 ml 0.1 N NaOH. Calculated: 2.01, 3.65 ml.

N-(N-Benzoyl-3-phenylalanyl)-β-chloroalanine Methylamide.

a) The N-(N-benzoyl-3-phenylalanyl)serine methylamide (0.8 g) was dissolved in 3 ml of thionyl chloride cooled to 0° and then allowed to stand for 1 hour in the cold. After treatment with 25 ml of ether there was obtained 0.9 g of white amorphous substance with m. p. 135-137°. On standing it evolved sulfur dioxide gas. The substance gave a copious precipitate of silver chloride with silver nitrate. Under the influence of water it was converted into the starting methylamide of N-(N-benzoyl-3-phenylalanyl)serine. Apparently, this compound was the β-chlorosulfinyl derivative of the methylamide of N-(N-benzoyl-3-phenylalanyl)alanine. The compound was not studied further.

b) The chlorosulfinyl derivative (0.8 g) of the methylamide of N-(N-benzoyl-3-phenylalanhl)alanine was dissolved in 5 ml of acetic acid heated to 100°, after which the solution was treated with 5 ml of water. Cooling gave needle crystals of the methylamide of N-(N-benzoyl-3-phenylalanyl)-β-chloroalanine. M. p. 199°. The substance is not described in the literature.

Found %: Cl 9.10, 9.08; N 10.82, 10.92. $C_{20}H_{22}O_3N_3Cl$. Calculated %: Cl 9.16; N 10.84.

c) The methylamide (0.8 g) of N-(N-benzoyl-3-phenylalanyl)-serine was mixed with 3 ml of thionyl chloride and heated at 60° until dissolved. To the reaction mixture after 14 hours was added 20 ml of ether. Here 0.85 g of the methylamide of N-(N-benzoyl-3-phenylalanyl)-β-chloroalinine separated. After recrystallization from a mixture of alcohol and butyl acetate the m.p. was 199-200°. Its mixted melting point with the compound described in Experment "b" failed to be depressed.

d) A mixture of 0.8 g of the methylamide of N-(N-benzoyl-3-phenylalanyl)serine and 0.17 g of phosphorus pentachloride in 10 ml of chloroform was stirred at room temperature to almost complete solution. Treatment with ether gave needle crystals, which were recrystallized from aqueous acetic acid. The yield of the methylamide of N-(N-benzoyl-3-phenylalanyl)-β-chloroalanine was 0.2 g. Its mixed melting point with the preparation described in Experiment "b" failed to be depressed.

e) A solution of 0.9 g of the methylamide of N-(N-benzoyl-3-phenylalanyl)serine in 5 ml of anhydrous alcohol was saturated under cooling with hydrogen chloride, and then heated for 1.5 hours at 70°. After removal of the alcohol the oily residue was made to crystallize by rubbing with ether, and the thus obtained crystals recrystallized from aqueous acetic acid. The yield of N-(N-benzoyl-3-phenylalanyl)-β-chloroalanine was 0.6 g. M. p. 198°. Its mixed melting point with the preparation obtained in Experiment "b" fails to be depressed. Evaporation of the mother liquor and recrystallization of the obtained crystals from 50% alcohol gave 0.1 g of the benzoylphenylalanine ester.

f) A solution of 0.2 g of the methylamide of N-(N-benzoyl-3-phenylalanyl)serine in 5 ml of dioxane was saturated with hydrogen chloride and allowed to stand for 2 hours at room temperature. After evaporation of the dioxane in vacuo the oily residue was treated as in Experiment "e". The yield of the methylamide of N-(N-benzoyl-3-phenylalanyl)-β-chloroalanine was 0.1 g, m. p. 195°. Its mixed melting point with the preparation obtained in Experiment "b" failed to be depressed.

The methylamide (0.2 g) of N-(N-benzoyl-3-phenylalanyl)-β-chloroalanine was heated for 2 hours at 100° with 4 ml of 50% alcohol. Reduction to small volume gave crystals of the methylamide of N-(N-benzoyl-3-phenylalanyl)serine. Its mixed melting point with the synthetic product failed to be depressed. The filtrate, remaining after removal of the methylamide of N-(N-benzoyl-3-phenylalanyl)serine, failed to show the presence of amino nitrogen.

Migration of the Peptide Residue Under the Influence of Concentrated HCl

a) Comparison of the Hydrolysis Rates of the N-Peptides and N,O-Peptides of Serine. The weighed samples of the serine N-peptides and N,O-peptides were each treated with 0.5 ml of hydrochloric acid (d 1.19) and then allowed to stand in the thermostat at 18 and 26°. After definite time intervals the amounts of amino nitrogen in an aliquot portion of the solution were determined by the Van Slyke method. The analysis results are given in Table 2.

b) Determination of the Amount of Serine in the Hydrolyzate. The isopropyl ester (0.4004 g) of N-(N-benzoyl-3-phenylalanyl)serine was hydrolyzed with concentrated hydrochloric acid at 26° for 6 hours. The solution was made up of 25 ml, and the amount of serine in 2.5 ml was determined by the periodate method.

For binding the ammonia there was consumed: 2.01 and 1.98 ml of 0.025 N H_2SO_4. Found serine in %: 20.1, 19.8.

The amount of amino nitrogen in an aliquot portion of the solution was determined by the Van Slyke method.

The amount of evolved nitrogen: 1.77 and 1.72 mg. Found amino groups in % : 28.26.

Influence of Concentrated Sulfuric Acid on the N-Peptide Derivatives of Serine

The weighed samples of the isopropyl ester of N-(N-benzoyl-3-phenylalanyl)serine, the methylamide of N-(N-benzoyl-3-phenylalanyl)serine and the methylamide of N-[N-(p-toluenesulfonyl)-glycyl]serine [6] were treated with sulfuric acid under the conditions given in Table 2. After definite time intervals the amounts of amino nitrogen in the solutions were determined by the Van Slyke method. An aliquot portion of the solution was treated under strong cooling with 20% alkali solution to pH 1-2, and then with 0.2 N alkali solution to pH 8.5, after which the amount of amino nitrogen present was again determined. The determination results are given in Table 3.

TABLE 3

Weight* (in g)	Acid treatment conditions	Conditions of alkali treatment	Amino nitrogen** (in %) of the sample weight	Amino nitrogen** (in %) of total N
	N-(N-Benzoyl-3-phenylalanyl)serine Isopropyl Ester			
0.0229	Heating with oleum for 2 minutes at 50°	–	1.73, 1.42	50, 42*
		pH 8.5, 18°	0.83, 0.83	23, 25
0.0319	10 minutes at 50° with 100% H_2SO_4	–	0.80, 0.83	23, 23.5
		pH 8.5, 18	0.60, 0.60	17, 17
0.0198	72 hours at 18° with 100% H_2SO_4	–	1.51, 1.37	43, 39
		pH 8.5, 18	0.86, 0.94	24, 27
0.0125	48 hours at 18° with oleum	–	1.58, 1.42	45, 41
		pH 8.5, 18	0.92	26
0.0236	3 hours at 50° with 100% H_2SO_4	–	2.71, 2.77	77, 79
		pH 8.5, 18	1.51, 1.51	43, 43
0.0186	0.14 N sulfuric acid solution in anhydrous dioxane for 3 hours on the water bath and overnight at room temperature	–	3.62, 3.75	103, 109
		pH 8.5, 18	3.64	104
0.0079	2 hours at 50° with 0.147 N H_2SO_4 in anhydrous dioxane	–	3.8, 3.66	110, 106
		pH 8.5, 18	3.7	107
0.0175	12 hours at 18° with 0.1 N H_2SO_4 in anhydrous dioxane	–	1.88, 2.15	62, 61
		pH 8.5, 18	2.02	58
	N-(N-Benzoyl-3-phenylalanyl)serine Methylamide			
0.0959	Conc. H_2SO_4 for 1 hour at 50°	–	6.9, 7.6	102, 110
		pH 9, 18°	5.2, 4.3	75, 61
0.2900	5.35 ml of 0.14 N H_2SO_4 in dioxane, 1 hour at 100°	–	5.4, 5.4	70, 71
		pH 9, 18	1.4, 1.4	33, 30
0.2900	5.35 ml of 0.14 N H_2SO_4 in dioxane, 2 hours at 100°	–	4.8, 5.0	64, 66
		pH 9, 18	2.3, 2.0	31, 30
	N-[N-(p-Toluenesulfonyl)glycyl]serine Methylamide			
0.3556	8 ml of 0.14 N H_2SO_4 in dioxane at 100° for 1.5 hours	–	3.6, 3.9	50, 55
		pH 9, 18°	0.45, 0.5	6, 7
0.3556	8 ml of 0.14 N H_2SO_4 in dioxane at 100° for 2.5 hours	–	4.5, 0.5	70, 71
		pH 9, 18	1.3, 1.3	38, 36

* The weight corresponds to the aliquot portion taken for determination of the amino nitrogen.

** The amino nitrogen, corresponding to the complete conversion of the N-peptide of serine into the O-peptide, is taken as 100 %.

SUMMARY

The reaction for the migration of the acylaminoacyl (peptide) residue in peptide derivatives of serine was studied. When the peptide derivatives of serine are reacted with thionyl chloride, or with hydrogen chloride in either alcohol or dioxane solution, the β-chloro derivatives of the peptides of alanine are formed, which in aqueous medium are converted into the original compounds. Under the influence of concentrated hydrochloric acid there apparently occurs migration of the peptide residue from nitrogen to oxygen, since the N-peptides of serine are hydrolyzed more rapidly than are the N,O-peptides. Two reactions are observed when the peptide derivatives of serine are treated with either sulfuric acid or oleum – the migration of the acylaminoacyl residue from nitrogen to oxygen, and the dehydration of the serine peptides.

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